DISTURBANCES IN GASTROINTESTINAL MOTILITY

Disturbances in Gastrointestinal Motility. . . .

DIARRHEA

CONSTIPATION

BILIARY DYSFUNCTION

Edited by

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PREFACE

THIS publication is based on a program of lectures and symposia entitled "Pathophysiology and Treatment of Disturbances in Gastrointestinal Motility" encompassing constipation diarrhea and biliary dysfunction which was held at the University of California School of Medicine in San Francisco on December 7 8 and 9 of the year 1958 under the combined auspices of the University of California School of Medicine and Continuing Education The expenses of the program were defrayed in part by a grant from the Purdue Frederick Company of New York City

The first portion of the program was devoted to some general considerations of the gastrointestinal tract and exposition of certain basic concepts of pertinent physiology pharmacology and psychodynamics The second part was concerned primarily with diagnosis and current therapy of various diseases and disorders Two panel discussions which were tape recorded during the program have been edited and are reproduced here with only minor changes

The purpose of the program was to advance basic knowledge in the field of gastrointestinal motility since disturbances in motility represent some of the most common the most controversial and the most difficult areas of treatment in all of gastroenterology It was felt that this purpose could best be realized through a meeting of outstanding gastroenterologists and specialists in related fields At this meeting it was intended that the participants review the status of current therapy and evaluate currently used experimental diagnostic methods

The participants who represented a number of outstanding

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medical institutions in the United States and England were invited because of their clinical experience and judgment as well as their original contributions to gastroenterology Although some of the concepts discussed at the meeting and included in this publication may be of a controversial nature it was the editorial policy to reproduce papers essentially as given

In the interest of ease in reading trade names of products are sometimes used instead of their descriptive or chemical identifications However endorsement of named products is not necessarily intended nor is lack of mention of similar products intended as criticism of them

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DISTURBANCES IN GASTROINTESTINAL MOTILITY

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MOTILITY OF THE ALIMENTARY CANAL OF MAN

NICHOLAS C HIGHTOWER JR M D Ph D *

FUNCTIONS of the gastrointestinal tract may be divided into absorption secretion and motility During the past decade there has been considerable advancement of our knowledge in each of these areas This progress primarily has been due to the development of techniques for studying these functions in the intact man The advent of radioactive isotopes has provided us with methods for studying absorption and secretion and the mechanisms of these processes have been elucidated to a considerable extent The development of techniques for accurate and continuous recording of gastrointestinal intraluminal pressure has provided new tools to investigate motor activity

The application of these new methods not only has increased our understanding of the physiology of the gastrointestinal tract but has opened many avenues of new research This has been particularly true for the motor activity of the esophagus In addition to intraluminal pressure measurements fluorocinematography is another new technique for studying motor activity of the gastrointestinal tract that offers considerable promise [1]

Gastrointestinal motility is frequently disturbed by disease of this organ system In fact most of the major diseases of the alimentary canal are manifest by a disturbance of motor activity Dysphagia vomiting retching crampy abdominal pain diarrhea

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ethylene catheters* (inside diameter 0 047 inches wall thickness 0 010 inches) to the strain gauge Recently these catheters have been made radiopaque and this provides for their localization during the examination by fluoroscopy The signal from the strain gauge energizes a sensitive galvanometer † and a continuous record is made on a photokymograph ‡ The system is powered by direct current from 6 volt storage batteries Respiration is recorded by a pneumograph about the lower part of the subject s chest Action potentials of the superficial muscles of the anterior neck are recorded by electromyographic electrodes and serve to indicate the onset of deglutition when recording from the pharynx and esophagus

For recording pressures during swallowing three of the small polyethylene catheters have been used with their open tips in tandem separated by a distance of two to five cm (fig 1) The

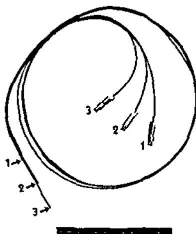


Fig 1 Radio-opaque catheters used to record intraluminal pressure The catheters are bound together at intervals with silk thread and the tips are separated by a distance of 2 to 5 cm Medal adapters at proximal end connect catheter to pressure transducer

*PE 190 Clay Adams Inc New York N Y
†Mod 1 40 350C Heiland Corp Denver Colorado
‡Waters Corp Rochester Minn

and constipation are examples of symptoms produced by altered motility

The types of motor activity of the alimentary tract can be divided into mixing peristalsis and tonus changes [2] In the presentation of this material an attempt will be made to correlate the various types of motor activity observed in each of the areas of the alimentary canal to these particular descriptive functional terms Various parameters as amplitude of pressure duration and rhythmical occurrence of each type of motor activity will be given In addition the influence of various pharmacological agents on gastrointestinal motility will be presented The effect of disease on motility of the alimentary canal of man will be mentioned only briefly as this topic will be discussed in detail in another section of this book *

METHODOLOGY

Two techniques of recording motor activity from the alimentary canal have been used in our laboratory One provides for the accurate and continuous recording of intraluminal pressures through small fluid filled open tipped catheters [3] The other method is a water filled balloon system [4] In the balloon system motor activity is transmitted from the balloon to a small air filled glass spoon manometer and a record is obtained on a photokymograph as in the direct pressure measuring system The direct pressure measuring technique has been used to great advantage in studying the motor activity of the pharynx and esophagus The balloon system has been used primarily for studying motor activity of the remainder of the alimentary canal

Direct Pressure Measuring System Pressure transducers with adequate dynamic characteristics are available for accurately recording intraluminal pressure changes In our laboratory we have used the strain gauge type of transducer† and found it very satisfactory Pressure is transmitted through small fluid filled poly

* Bargen J Arnold *Disturbances of Gastrointestinal Motility Associated with Systemic Disease* pp 317 334

† Model P 23 D Statham Instruments Corp Los Angeles 64 Calif

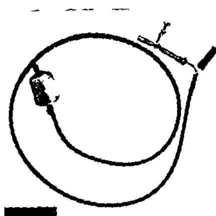


Fig 3 Balloon system used to record motility from the stomach and upper small bowel The perforations into one lumen of the double lumen tube just proximal to the balloon provide for sampling gastric or intestinal contents

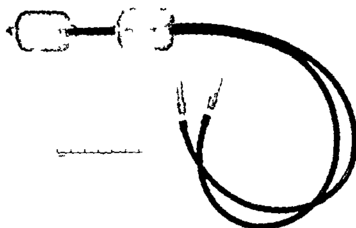


Fig 4 Tandem system of ballons used for recording motor activity from the lower ileum and colon through enterostomy stomata and from the rectum and sigmoid

catheters are bound together at intervals with silk thread Metal adapters* are employed to connect the polyethylene tubing to the

* No A 2625 Size C Clay Adams Inc New York



Fig 2 Illustrating technique for recording esophageal motility Syringe with stopcock manifold in foreground is for flushing system Transducers are mounted on ring stand behind fluoroscopic table The photokymograph is in background (From Hightower N C Jr The physiology of symptoms I Swallowing the esophageal motility *Am J Dig Dis* n s 3 562 1958 Reproduced with kind permission of the editors of *American Journal of Digestive Diseases*)

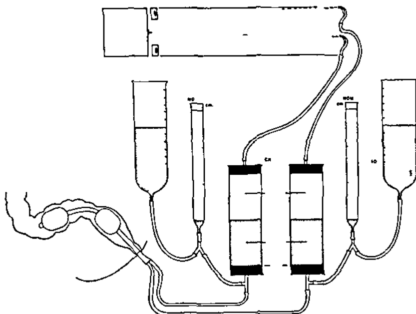


Fig 6 Diagram of balloon method of recording motility Each balloon is connected to a separate filling system When recording with one balloon only one system is used After balloon is filled with water the manometer and reservoir are clamped off from the system

no change of characteristics over long periods of time They respond linearly to a wide range of pressures and are unaffected by humidity and temperature Increases in pressure in the spoon tend to straighten out its concavity and decreases in pressure tend to increase it

The apparatus used for controlling the volume of air and water in the recording system is illustrated in figure 6 This apparatus is used to connect the balloon in the gastrointestinal tract to the glass spoon manometer on the photokymograph The apparatus consists of a calibrated pressure chamber of 200 ml capacity a reservoir for filling the system and a calibrated manometer for measuring the pressure of the system when filled By varying the amount of water in the pressure chamber the volume of air in the recording system is altered and this governs the volume pressure coefficient of the system As ordinarily used the

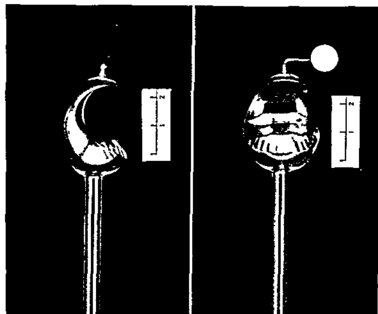


Fig 5 Pyrex glass manometer used in the balloon method of recording The small concave mirror with a focal length of 100 cm is attached to the tip of the manometer with a bit of wax

strain gauge At intervals during the recordings the tubes are flushed from a syringe controlled by a series of stopcocks (fig 2)

Balloon Method for Recording Motility Sawyer balloons* which are symmetrical in shape measure 5 cm in length and have a diameter of 3 cm are used The balloons have a capacity of approximately 35 ml without producing distention of the latex For recording motor activity from the stomach and upper small bowel a single balloon is usually employed (fig 3) For recording motor activity from the terminal ileum and colon through enterostomy stomas and from the rectum and sigmoid a tandem system of balloons is used as illustrated in figure 4

Pyrex glass spoon manometers as described by Kubicek Sedgwick and Visscher are used in the balloon system of recording (fig 5) When properly constructed these manometers have been found to be extremely sensitive display little hysteresis and show

* V Mueller & Co Rochester Minn

of patients all medication was discontinued 24 hours before the study The subject was placed usually in the supine position on the fluoroscopic table When recording from the pharynx esophagus stomach or upper small bowel the catheters or balloons were swallowed When recording from the rectum and sigmoid colon the catheters and balloons were inserted under direct vision through a sigmoidoscope In patients with enterostomy stomas the tubes were inserted in a cephalad direction through the ileostomy or colonic stoma In most instances recordings continue for two hours or longer After an appropriate controlled period of observation food or drugs were administered When recording from the pharynx and esophagus a liquid and a solid bolus were used to record deglutition patterns

Analysis of Records Motility records obtained from all parts of the alimentary canal have been subjected to a quantitative analysis In general the system of nomenclature as used by Adler Atkinson and Ivy [8] has been applied to the various wave patterns that are recorded from each of the areas of the alimentary canal Motility waves were designated as Type I II III or IV This system of terminology was originally adopted because it did not have a functional implication The designation of individual waves into types has served well in all portions of the alimentary canal except in the pharynx and esophagus

The quantitative analysis of motility records has provided an accurate method for determining the types of motility present in various parts of the alimentary canal as well as demonstrating the effects of disease surgical procedures and drugs on motor activity [9-13] It is important that the recording be continued for a long enough period in order to obtain a representative estimate of the quantity and quality of motor activity present When studying the effects of drugs the control period of observation should be at least one hour

The records were first examined to classify the motility waves into types The amount of time each type of motor activity was present was expressed as per cent of time of observation Total activity for the period of observation was also determined When drugs or food were administered the recording was con

system contains approximately 120 ml of air This provides a volume pressure coefficient of 0 134 and allows 2 ml of water to be expressed from the balloon by each 15 cm of water pressure

The balloon in the gastrointestinal tract is filled under a pressure of 15 cm of water It has been found that this filling pressure is adequate to overcome the basal intraluminal pressure in all parts of the gastrointestinal tract[6] (Table I) This filling pressure does not produce distention of the balloon A filling pressure of 15 cm of water produces the following average volumes of water in the balloon when located in different parts of the gastrointestinal tract stomach 28 ml duodenum 16 ml jejunum 20 ml ileum 24 ml and colon 22 ml [4]

TABLE I
BASAL INTRALUMINAL PRESSURE IN VARIOUS PARTS OF GASTROINTESTINAL TRACT

Part of G I Tract	*No Subjects*	*Basal Pressures (cm H_2O) Mean*
Lower Esophagus	12	− 5 5
Cardia Stomach	6	+ 6 2
Body Stomach	4	+ 6 5
Antrum Stomach	6	+ 7 8
Prox Small Bowel	4	+ 8 1
Dist Small Bowel	4	+ 7.5
Desc Colon	6	+ 9 0
Rectosigmoid	2	+10 4

(From Hightower N C Jr Determination of basal intraluminal pressures in alimentary canal of man *Federation Proc* 26 67 1953)

It should be pointed out that this system of recording provides for the registration of balloon pressure and not true intraluminal pressure on the photokymographic film It has been demonstrated however that in most parts of the gastrointestinal tract the simultaneous pressures recorded by the balloon method and the direct pressure measuring method agree well [7]

Procedures All normal individuals and patients who have reported to the laboratory for motility studies have fasted for 8 12 hours Liquids by mouth and smoking before reporting to the laboratory on the day of the test was not permitted In the case

of patients all medication was discontinued 24 hours before the study The subject was placed usually in the supine position on the fluoroscopic table When recording from the pharynx esophagus stomach or upper small bowel the catheters or balloons were swallowed When recording from the rectum and sigmoid colon the catheters and balloons were inserted under direct vision through a sigmoidoscope In patients with enterostomy stomas the tubes were inserted in a cephalad direction through the ileostomy or colonic stoma In most instances recordings continue for two hours or longer After an appropriate controlled period of observation food or drugs were administered When recording from the pharynx and esophagus a liquid and a solid bolus were used to record deglutition patterns

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The records were first examined to classify the motility waves into types The amount of time each type of motor activity was present was expressed as per cent of time of observation Total activity for the period of observation was also determined When drugs or food were administered the recording was con

tinued for another hour or so and a comparison was made between a statistical analysis of the control and test periods of observations

Pressures of the Alimentary Canal Intraluminal pressures recorded from the alimentary canal can be divided into four types depending upon their origin[14] (1) *Basal pressure is defined as that pressure existing within the lumen when there is an absence of motor activity (fig 7)* In all parts of the alimentary canal except the normal esophagus this was a positive pressure (Table I) When the basal pressure was measured on 70 records obtained from 44 subjects the mean basal pressure

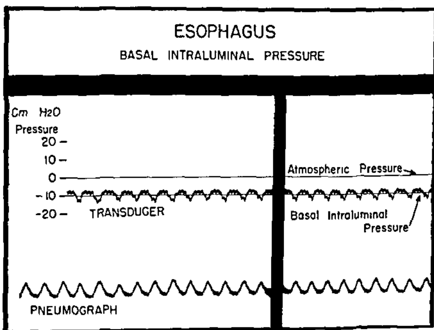


Fig 7 Basal intraluminal pressure in lower third of esophagus To determine basal intraluminal pressure a line is drawn through the phasic pressure variations produced by respiration and cardiovascular pulsations Note decrease of esophageal pressure with inspiration (upward deflection of pneumograph) and increase in esophageal pressure with expiration (From Hightower N C Jr Olsen A M and Moersch H J A comparison of the effects of *Acetyl beta methyl choline Chloride (Mecholyl) on esophageal* intraluminal pressure in normal persons and patients with cardiospasm *Gastroenterology* 26 592 1954 Reproduced with kind permission of editors of *Gastroenterology*)

in the esophagus was −5.5 cm water. In other parts of the alimentary canal the mean basal pressure varied from +6.2 cm water in the cardia of the stomach to +10.4 cm water in the rectosigmoid.[f] Basal pressure may be influenced by a number of factors as intrathoracic or intra-abdominal pressure, the tonus of the muscular walls of alimentary canal, position of the subject, and compression or traction upon the gut of adjacent organs and structures. (2) *Respiratory movements* produced changes in intraluminal pressure in all parts of the alimentary canal. These pressure changes were greatest in the esophagus (Table II). (3) *Cardiovascular pulsation* also produced intraluminal pressure changes. As with respiration, these changes in pressure were most marked in the esophagus (Table III). (4) *Motor activity* due to peristalsis, segmentation, or tonus changes also altered intraluminal pressure.

The recognition and detailed analysis of intraluminal pressures provides for a better understanding of the motor physiology of the alimentary canal.

TABLE II

RESPIRATORY PRESSURE CHANGES RECORDED FROM VARIOUS PARTS OF GASTROINTESTINAL TRACT

Part of G.I. Tract	*No. Subjects*	*Respiratory Pressures (cm.H₂O) Mean*
Lower Esophagus	10	7.9
Cardia Stomach	8	3.2
Body Stomach	6	4.2
Antrum-Stomach	17	3.9
Prox. Small Bowel	6	3.2
Dist. Small Bowel	3	0.9
Desc. Colon	6	2.4
Rectosigmoid	3	1.5

(From Hightower, N. C., Jr.: Determination of basal intraluminal pressures in alimentary canal of man. *Federation Proc.*, 12: 67, 1953.)

PHARYNGEAL MOTILITY

Pharyngeal motility represents the second stage of deglutition. This stage of deglutition is concerned with the transport of swallowed material from the oral cavity through the pharynx to

the esophagus The first stage of deglutition is the voluntary act of forcing liquid or a bolus of food into the pharynx The second stage of deglutition or transport of material through the pharynx *is entirely reflex in nature This is a highly complicated and inte* grated stage of deglutition and the entire stage requires only a few tenths of a second [3] The third stage of deglutition is trans port of a swallowed material through the esophagus

TABLE III

Cardiovascular Pressure Changes Recorded from Various Parts of Gastrointestinal Tract

Part of G I Tract	*No Subjects*	*Respiratory Pressures (Cm H O) Mean*
Lower Esophagus	11	2 6
Cardia Stomach	7	0 6
Body Stomach	6	0 3
Antrum Stomach	16	0 4
Prox Small Bowel	9	0 7
Dist Small Bowel	2	0 2
Desc Colon	5	0 2
Rectosigmoid	3	0 4

(From Hightower N C Jr Determination of basal intraluminal pressures in alimentary canal of man *Federation Proc* 12 67 1953)

Description of Pharyngeal Motor Activity The contact of material from the mouth with pharyngeal and peripharyngeal structures initiates reflexes that complete the second and third stages of deglutition The base of the tongue tonsils anterior and posterior pillars of the fauces soft palate uvula and the posterior pharyngeal wall are all sensitive areas which when stimulated by tactile stimuli will initiate the swallowing reflexes Cocainization of these structures inhibit the swallowing reflexes The principal nervous pathway is the glossopharyngeal nerve

The swallowing act once initiated is dominant over other functions occurring in this area thus respiration and speech are interrupted by the second stage of the swallowing act The complexity of the act and high degree of integration necessary is appreciated when one recalls the time sequence of events in this stage of deglutition The entire act is completed in approximately

one second and during this time a number of events as described below must be accomplished

To allow the swallowed material to continue on its intended course into the esophagus it is necessary that other pathways into the pharynx be closed A number of almost simultaneous actions occur The swallowed material is prevented from re entering the mouth by the tongue which remains retracted and elevated against the hard palate and also by the contraction and approximation of the posterior pillars Above the naso pharynx is sealed off by the elevation of the soft palate as it comes in contact with the posterior pharyngeal wall The en trance into the larynx and trachea is effectively closed by the elevation and forward movement of the larynx due mainly to the action of the anterior portions of the suprahyoid musculature The larynx thus comes to rest under the base of the tongue This action also increases the anterior posterior diameter of the pharynx The epiglottis is bent backwards and both the true and false vocal cords are approximated further sealing the re spiratory pathway

At the beginning of these events contraction of the superior pharyngeal constrictor occurs A rapid peristaltic wave moves down the pharynx propelling the bolus in front of it The walls and structures of the hypopharynx are elevated to engulf the oncoming bolus The cricopharyngus muscle which has kept the esophagus closed until now relaxes as the bolus approaches and allows it to enter the upper esophagus The peristaltic contrac tion passes over the pharyngoesophageal junction and continues into the esophagus to become the primary esophageal peristaltic contraction

Pharyngeal Pressures It has been only recently that pharyn geal pressures have been recorded with systems of adequate dynamic characteristics to allow interpretation of the pressure changes Fyke and Code[1] have used a small differential trans former[16] attached to the end of a gastric tube for a pressure transducer and have recorded pressures from the pharynx pharyngoesophageal junction and the upper esophagus Their

method of recording has been described previously and has been used to record accurate and continuous pressures from all major areas of the alimentary tract [14]

In our laboratory we have confirmed their findings The typical pressure changes occurring in the pharynx during the second stage of deglutition are illustrated in figure 8 In the pharynx basal resting pressure is positive It usually amounts to 3 10 cm of water pressure With the initiation of the swallow small variable pressure changes are recorded These changes which precede the onset of the large positive pressure wave are 0 3 to 0 5 seconds duration and they probably are produced by the preparatory actions of the peripharyngeal structures in anticipation of the peristaltic wave of the pharyngeal constrictors With the onset of the peristaltic contraction of the superior pharyngeal constrictor the large positive pressure wave is produced By using three recording tubes in tandem the rate of progress of this pharyngeal peristalsis is determined easily In the pharynx the maximum rate of propagation of the peak pressure produced by the peristaltic contraction has been found to be from 40 50 cm per second [1] The duration of the large positive wave produced by pharyngeal peristalsis varies from 0 5 to 0 8 seconds The magnitude of the pressure wave is usually from 50 100 cm of water pressure [3]

The small short negative deflections so frequently observed following the large positive wave are of interest and have not been explained satisfactorily They cannot be related to the large negative wave that develops at the pharyngo esophageal junction because a high pressure head created by the descending pharyngeal peristalsis is interposed (fig 8) This small negative component probably is related to a slight vacuum created by the peristaltic wave sweeping the swallowed material down the pharynx After passage of the peristaltic wave the peripharyngeal structures remain in their fixed positions momentarily providing for the development of a slight negative pressure The negative component of the complex is terminated suddenly as air re enters the pharynx from above through the nasal cavity as the soft palate falls away from the posterior pharyngeal wall The dura

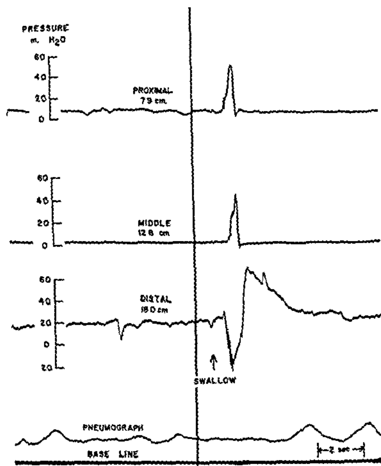


Fig 8 Intraluminal pressure changes in the pharynx and pharyngo esophageal junction during deglutition The distance from the incisor teeth to tip of each catheter is indicated The zero of each scale is atmospheric pressure Proximal and middle catheters are recording from the pharynx The distal catheter is recording from the high pressure zone of the pharyngo-esophageal junction Respiration ceased voluntarily immediately before deg lutition Note high basal pressure at pharyngo esophageal junction With deglutition a large negative pressure wave develops in the junctional zone which not only obliterates the high basal pressure but falls below atmos

tion of the terminal negative component is usually only 0 1 0 2 seconds and its negative deflection is usually 4 8 cm of water below the basal pressure [3]

Disturbances of Pharyngeal Motility by Disease A disturbance of pharyngeal motility results in dysphagia due to interference with the second stage of deglutition A number of infections neoplastic and neurologic diseases both local and systemic are capable of producing dysphagia by interfering with the second stage of deglutition By far the most common cause of dysphagia involving this stage is acute pharyngitis Peritonsillar and retropharyngeal abscess mumps, scarlet fever diphtheria and acute thyroiditis are all associated with dysphagia Fixation of the larynx by chronic inflammatory processes such as tuberculosis and syphilis may make swallowing extremely difficult Neoplasms of the larynx or thyroid may also produce fixation of the larynx thus preventing its upward and forward movement as normally occurs during the second stage of deglutition Mobility of the larynx is essential to the second stage of deglutition Neoplasms of pharyngeal and tonsillar origin may mechanically block deglutition during the second stage

Pharyngeal paralysis is a common cause of dysphagia In such instances it may be impossible for the soft palate to be elevated thus allowing liquids to be regurgitated through the nose The pharyngeal constrictors may be unable to initiate the peristaltic contraction and empty the contents of the pharynx into the esophagus Pharyngeal paralysis usually results from bulbar lesions as seen in poliomyelitis multiple sclerosis cerebral vascular hemorrhage and syringomyelia Cranial nerve (glossopharyngeal) neuritis may also result in pharyngeal paralysis Myasthenia gravis is capable of producing dysphagia due to disturbance of this stage of deglutition Palatal and pharyngeal paralysis sometimes follows diphtheria

ESOPHAGEAL MOTILITY

Esophageal motility is concerned with the third stage of deglutition Its function is to transport material introduced into it from the pharynx on into the stomach Because the esophagus

passes through the thoracic cavity sphincteric mechanisms are necessary at either end to separate the positive intraluminal pressure of the pharynx and stomach from the negative intraluminal pressure of the esophagus These junctional regions have been described anatomically by Lerche[18] and delineated physiologically by Fyke and Code[1 19]

Description of Esophageal Motor Activity In the normal individual three types of esophageal contractions have been described *The primary peristaltic contraction* as pointed out by Templeton [0] actually originates in the pharynx during the second stage of deglutition From the pharynx this peristaltic contraction travels over the pharyngo esophageal junction on into the esophagus in an unbroken manner and continues to the level of the diaphragm In the upper esophagus the rate of propagation of a peristaltic wave becomes progressively decreased as it descends the esophagus The faster rate of travel in the upper esophagus is thought to be due to the striated muscle which is found here [1] By actual measurement of the rate of propagation of the primary peristaltic wave we have found that there is a progressive decrease in the rate to a level about 25 cm distance from the incisor teeth The rate of propagation decreases progressively from a maximum of 40 50 cm per second to about 3 cm per second at this level The rate of propagation then increases over the next 10 cm of the distal esophagus—that is from about 24 to 34 cm distance from the incisor teeth In this area the rate increases to about 8 to 10 cm per second Below this level there is again a rapid decrease in the rate of propagation until at about 40 42 cm distance from the incisor teeth the rate of propagation is 1 cm per second or less[17] (fig 9)

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phenic pressure This occurs while pressure recorded from tip of middle catheter 2 cm proximal in the pharynx is increasing Camera speed 10 mm per second (From Hightower N C Jr The physiology of symptoms I Swallowing and esophageal motility *Am J Dig Dis* n s 3 562 1958 Reproduced with kind permission of the editors of *American Journal of Digestive Diseases*)

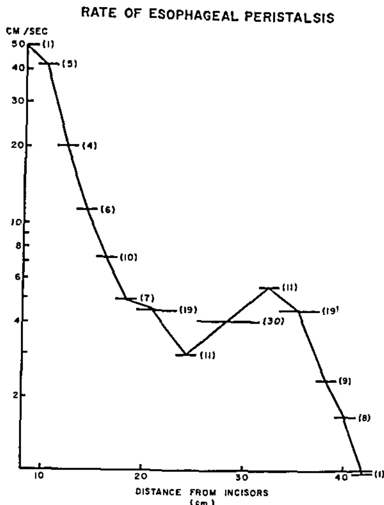


Fig 9 The rate of propagation of the primary peristaltic contraction in the pharynx and esophagus as determined in 15 healthy adults The number of observations at each level are indicated in parenthesis The short horizontal lines indicate the distance over which the groups of observations were made (From Hightower N C Jr and Sulem M E The rate of pharyngeal and esophageal transport *J Lab & Clin Med* 52 820 1958)

The mechanism of production of the primary peristaltic contraction is entirely reflex The afferent limb of the reflex arc is principally the pharyngeal branches of the glossopharyngeal nerve The efferent limbs of the reflex arc are the vagi Central

connections of the arc are thought to be in the medulla in the neighborhood of the vagus nucleus Certain observations indicate that there is considerable central integration responsible for the orderly manner in which the primary peristaltic wave descends down the esophagus For example when a primary wave approaches a local pathological process such as an annular carcinoma of the mid esophagus interrupting the local muscular and neural elements the peristaltic wave ceases upon reaching the lesion only to be observed a moment later appearing below the lesion and continuing on toward the stomach [0] Local neural connections the Auerbach plexuses also are important in the propagation of the primary peristaltic wave

Secondary peristaltic contractions occur in the normal esophagus in response to distention The distention may be localized such as that produced either by a solid bolus of food or experimentally in response to the distention of a small balloon placed in the esophagus Kramer and Ingelfinger have determined the average rate of occurrence of secondary contractions induced by a small disteneded balloon and found it to be 6 5 and 8 1 waves per minute in the upper middle and lower parts of the esophagus respectively Distention over a considerable portion of the esophagus as occurring with liquids also may result in the production of secondary peristaltic waves [0] When such contractions are observed roentgenoscopically they usually arise in the region of the arch of the aorta A segment of the esophagus is seen to undergo spontaneous contraction which forces barium both toward the mouth and the stomach The contraction wave then proceeds to move down the esophagus in a manner similar to the primary peristaltic wave That the secondary peristaltic wave is definitely propulsive in nature also has been demonstrated by balloon studies

Tertiary esophageal contractions have been observed and described in apparently normal individuals past middle age These contractions occur irregularly and locally and are observed in the lower esophagus They are not peristaltic Their function is not known Tertiary contractions occur rapidly and are of

brief duration Roentgenologically, they may produce a varied picture such as a serrated or beaded appearance, multiple diverticula like pockets and sometimes a picture which is referred to as curling and the corkscrew" esophagus It has been suggested that contractions of the spiral muscular coat of the lower esophagus account for these phenomena [18] Roentgenologically these contractions are observed to occur spontaneously Also at times they are seen to appear in the lower esophagus when a primary peristaltic wave has reached about the level of the aortic arch The peristaltic wave may stop at this level or continue down the esophagus to obliterate the tertiary contractions

Esophageal Transport As in other parts of the alimentary canal transport within the esophagus is dependent upon a gradient of pressure to move materials within the lumen In the esophagus the principal factor producing this pressure gradient is the primary peristaltic contraction In transport of a solid bolus the primary peristaltic contraction is of particular importance It sweeps the bolus ahead of it as it progresses from the upper to the lower esophagus If the primary peristaltic wave is ineffective due to the size consistency or dryness of the bolus secondary peristaltic contractions may occur which complete the transport of the bolus through the esophagus or another primary wave is initiated by deglutition The secondary contractions produced by bolus distention of the esophagus are initiated locally

The manner in which liquids are transported through the esophagus is dependent upon the position of the subject since gravity plays an important role In the upright position liquids may travel through the esophagus at a speed that greatly exceeds the rate of propagation of the primary peristaltic wave This rapid transfer of liquids to the lower end of the esophagus is considered to be due to the propelling force created by the contraction of the pharyngeal constrictors during the second stage of deglutition as well as by the action of gravity upon the swallowed liquid Thus from an area of positive pressure the liquid is more or less squirted into the lumen of the esophagus in which there is a negative pressure In the upright position the rapid passage of liquids through the esophagus requires only a few

tenths of a second and occurs while the esophagus is relaxed and before the primary peristaltic contraction in the esophagus has begun Fluoroscopy has shown that swallowed liquids are usually arrested at the lower end of the esophagus and await the arrival of the peristaltic contraction before they are admitted into the stomach At times however when a series of swallows occurs rapidly as when drinking a glass of water the liquid may pass on through the cardia with little pause and enter the stomach within a second or two after drinking has begun Almost every one has experienced this when drinking a very hot or very cold substance by becoming aware of an almost immediate feeling of cold or warmth in the epigastrium When a quick succession of swallows occurs the primary peristaltic wave is inhibited until the last swallow is finished The peristaltic wave then passes down the esophagus emptying any remaining contents

In either the supine or head down position the force of gravity is eliminated and the liquid bolus is handled in a manner similar to a solid bolus i e transport is dependent upon the primary peristaltic wave

The exact mechanism of esophageal evacuation into the stomach has been a matter of much dispute and still has not been clearly established Lerche[18] has postulated a mechanism of esophageal evacuation which is based on detailed anatomic studies and roentgenographic correlations His anatomical findings indicate the presence of two dilatations of the lower end of the esophagus as demonstrated in figure 10

The upper dilatation is called the esophageal ampulla and the lower one the gastro esophageal vestibule The ampulla is simply a bulbar dilatation of the lower end of the esophagus It is separated from the gastro esophageal vestibule by the inferior esophageal sphincter" The gastro esophageal vestibule is separated from the stomach by the constrictor cardiae which also is said to have a sphincteric action The intra diaphragmatic portion of the esophagus is the gastro-esophageal vestibule the diaphragm circling the vestibule at the level of about one cm below the inferior esophageal sphincter

Lerche believes the inferior esophageal sphincter normally remains tonically closed and opens mechanically or reflexly to the

peristaltic pressure above the ampulla After the inferior esophageal sphincter has opened, the ampulla contracts forcing its contents into the vestibule When the vestibule is filled being closed below by the constrictor cardiae the inferior esophageal sphinc

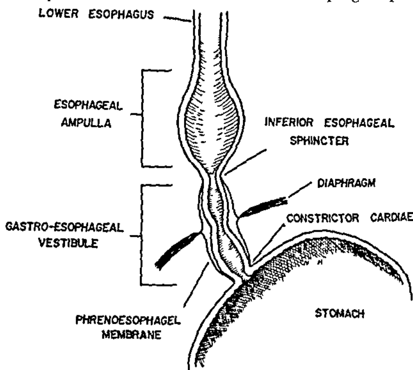


Fig 10 Schematic diagram of the esophagogastric junction according to Lerche [18] (From Hightower N C Jr The physiology of symptoms I Swallowing and esophageal motility *Am J Dig Dis* n s 3 562 1958 Reproduced with kind permission of the editors of *American Journal of Digestive Diseases*)

ter contracts The constrictor cardiae now relaxes and the vestibule contracts and shortens itself emptying its contents into the stomach

Physiological observations based upon pressures recorded from this area indicates that the entire vestibular region probably acts as a sphincteric mechanism [3]

Esophageal Pressures Esophageal pressures as determined by direct pressure measuring techniques have contributed greatly

to the understanding of the motor phenomena of the body of the esophagus as well as its sphincteric areas In the discussion to follow the pressures of the pharyngo esophageal junction the body of the esophagus and the esophagogastric junction will be considered separately

The pharyngo esophageal junction is characterized by a short zone of high resting intraluminal pressure in the region of the inferior pharyngeal constrictor or cricopharyngeus muscle at the level of the cricoid cartilage[31-33] Circular muscle fibers in this area remain in a state of tonic contraction[4,5] producing a zone of high resting intraluminal pressure and effectively separating the pharyngeal and esophageal lumina The zone of high pressure is approximately 4 cm in length and usually is located between 15 to 20 cm from the incisor teeth The basal resting pressure in the high pressure zone varies from 20 to 30 cm of water above atmospheric pressure (fig 11)

When intraluminal pressures are recorded from the pharyngo esophageal junction during deglutition the pattern of pressure change is distinctly different from that recorded from the pharynx or from the upper esophagus (figs 8 and 12) Immediately after the onset of deglutition usually within 0 5 seconds a small sharp positive wave develops Within 0 1 to 0 3 seconds maximum pressure is reached and is between 10 to 30 cm of water above basal pressure in the junctional zone Pressure then decreases rapidly below the basal pressure and usually becomes negative in comparison with atmospheric pressure

This marked decrease in pressure in the pharyngo-esophageal junction occurs almost simultaneously with the large increase in pressure in the pharynx produced by the peristaltic wave resulting from the contraction of the superior and middle pharyngeal constrictors The small initial positive wave observed in the pharyngo esophageal junction with deglutition may be due to an increase in the tonic contraction of the circular fibers of the cricopharyngeal muscle or it may be related to elevation of the larynx and increased tension on this area This small positive pressure wave occurs during the period that small variable pressure changes are observed in the pharynx immediately prior to the

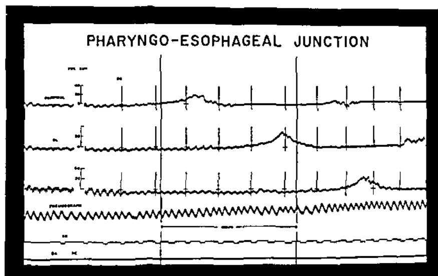


Fig 11 Demonstration of the zone of high pressure at the pharyngo esophageal junction The catheters were placed in the esophagus then with drawn slowly while recording continuously Each centimeter of withdrawal was indicated on the film by the signal Vertical lines indicate the distance in centimeters from the incisor teeth to the tip of each catheter This pull through technique clearly demonstrates the negative basal pressure in the esophagus and the zone of high pressure at the pharyngoesophageal junc tion Note that at approximately 17 cm from the incisor teeth the pressure rises in each tracing and returns to atmospheric pressure at approximately 14 cm as the tips of the catheters pass through the high pressure zone Camera speed 2 5 mm per second (From Hightower N C Jr The physiology of symptoms I Swallowing and esophageal motility *Am J Dig Dis* n s 3 562 1958 Reproduced with kind permission of the editors of *American Journal of Digestive Diseases*)

development of the high pressure pharyngeal peristaltic wave As the pharyngeal pressure increases the pharyngo esophageal junction pressure decreases thus greatly facilitating the develop ment of a high pressure gradient from the pharynx to the pharyngo esophageal junction The duration of the negative com *ponent of the junctional pressure pattern of deglutition is usually* 0 7 to 1 0 seconds after which time the pressure returns to the previous basal level The pressure continues upward however and another positive pressure wave forming a third component of the pattern is observed This positive pressure wave represents a continuation of the pharyngeal peristalsis through the pharyngo

esophageal junction The maximum pressure produced by this wave is usually from 70 to 90 cm of water above atmospheric pressure[3] Pressure then returns to the previous basal level within

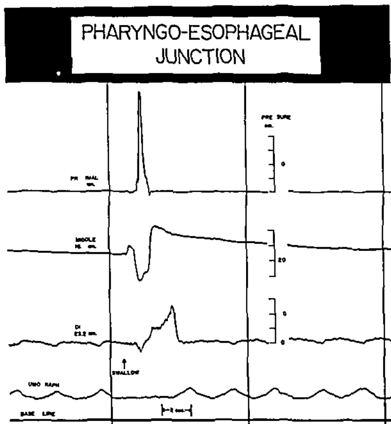


Fig 12 Proximal catheter is in the lower pharynx the middle catheter is in the pharyngoesophageal junction and the distal catheter is in the upper esophagus The sequential appearance of the peak pressure in each complex from above downward is indicative of the passage of the peristaltic contraction from the pharynx over the pharyngoesophageal junction into the upper esophagus After deglutition note the slow return to basal pressure in the junctional zone Respiration was voluntarily inhibited at the end of a normal expiration a few seconds before swallowing Camera speed 10 mm per second (From Hightower N C Jr The physiology of symptoms I Swallowing and esophageal motility *Am J Dig Dis* n s 3 562 1958 Reproduced with kind permission of the editors of *American Journal of Digestive Diseases*)

4 to 5 seconds or gradually, as shown in figures 8 and 12.

The complete integration of dynamics in the pharynx pharyngo esophageal junction and upper esophagus is precisely shown in figures 8 and 12. As the pharyngeal peristalsis approaches the esophagus the circular fibers of the cricopharyngeus muscle reflexly relax[4-9] promoting a high pressure gradient. With the arrival of the swallowed bolus at the pharyngo esophageal junction the previously relaxed fibers contract to propagate the peristaltic contraction and pressure gradient into the upper esophagus.

Pressures in the body of the esophagus may be discussed on the basis of their origin. In the normal esophagus the types of pressures that have been observed include (1) basal pressure which is the intraluminal pressure at the resting esophagus (2) respiratory and cardiovascular pressures which are transmitted to the lumen of the esophagus and are superimposed on the basal pressure and (3) pressures resulting from deglutition or spontaneous esophageal motor activity.

Basal intraluminal pressure has been defined as that pressure existing within the lumen of the esophagus when there is an absence of motor activity. Basal pressures determined by direct measuring methods have been found to be about minus 5 to minus 6 cm of water (Table I).

Superimposed upon the negative basal intraluminal pressure are pressure changes due to respiration and cardiovascular pulsations (figure 7). Inspiration produces a further increase in the negative intraluminal pressure while expiration decreases the negative intraluminal pressure. Respiratory pressure changes usually vary from 4 to 12 cm of water. In normal adults eupnic respiration produces a mean pressure change of 6 to 8 cm of water when recorded from the lower esophagus.[6,14] Changes in esophageal intraluminal pressure due to cardiovascular pulsations are usually quite constant in any one individual when recorded from one site but have been found to vary at different levels of the esophagus. In different individuals cardiovascular pressure may vary from 1.2 to 3.6 cm of water. When recorded

from the lower esophagus the mean pressure change which cardiovascular pulsations produce is 2 6 cm of water [6] Both respiration and cardiovascular pulsations produce a greater change in intraluminal pressure in the esophagus than any other site within the alimentary canal

Deglutition produces a characteristic pattern of pressure change in the normal esophagus The pressure pattern consists of an initial negative wave followed by three positive pressure components as illustrated in figures 13 and 14 The initial negative component is of brief duration and occurs immediately after the

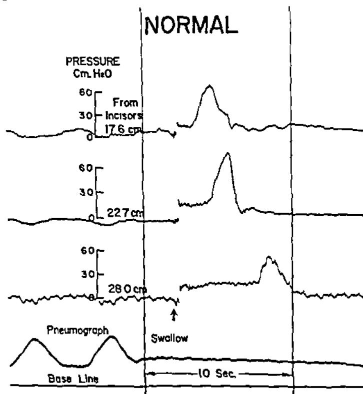


Fig 13 Normal deglutition pressure complexes recorded from upper esophagus Catheter tips are approximately 5 cm apart Note progressive prolongation of complex as recorded from each catheter from above downward Respiration voluntarily ceased at end expiration immediately prior to deglutition Camera speed 10 mm per second

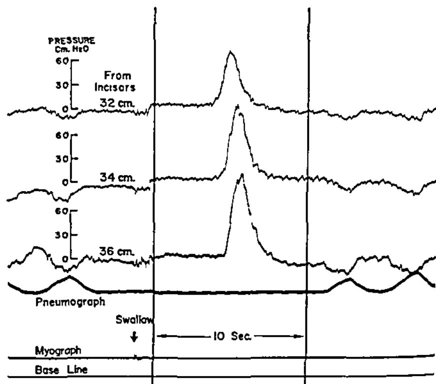


Fig 14 Normal deglutition pressure complexes recorded from lower esophagus Catheter tips are 2 cm apart Myograph indicates onset of deglutition Camera speed 10 mm per second

onset of deglutition It is observed more frequently in the upper than the lower esophagus and is thought to be due to the sudden stretching of the closed esophagus by elevation of the larynx [18, 19] The negative component is followed by an abrupt increase in pressure of 10 to 15 cm of water Following the abrupt rise in pressure the third component of the complex is observed This consists of a slowly increasing positive pressure change or a plateau of pressure as demonstrated in figures 13 and 14 The fourth and most prominent component of the deglutition pressure pattern is a large simple monophasic positive pressure wave that rises rapidly to a peak and declines with equal speed Thus immediately after deglutition pressure changes

are observed in the upper, middle, and lower esophagus that can be correlated with the approaching primary peristaltic contraction. The abrupt rise in pressure following the initial negative reflection has been attributed to the sudden injection of liquid into the esophagus.[8,9] The gradually increasing plateau of pressure is related to the approaching peristaltic contraction. Its duration is directly proportioned to the depth of the recording catheter in the esophagus. The large monophasic positive pressure wave that terminates the complex is recorded as the peristaltic contraction passes over the open tip of the catheter.

The magnitude of the large positive pressure wave terminating the deglutition complex has been carefully measured by a number of investigations.[14,26,28,29,33] In general, pressures of 40 to 100 cm. of water are produced, as indicated in Table IV. The duration of the wave varies from approximately 2 seconds in the upper esophagus to 6 seconds in the lower esophagus.

The secondary peristaltic contraction produces a pressure wave similar to the final pressure wave of the deglutition pressure pattern. It is a simple monophasic positive pressure wave that rises rapidly to a peak, then returns promptly to the baseline. Secondary waves are usually of less amplitude than primary waves.[7]

The esophagogastric junction is also characterized by a zone of high basal pressure. Only within the past few years have anatomists, physiologists, radiologists, and endoscopists been able to reach some common agreement and understanding of the structure and function of the esophagogastric junction. By radiologic and manometric studies Sanchez, Kramer, and Ingelfinger have demonstrated that the distal 2 to 5 cm. of the esophagus, Lerche's gastroesophageal vestibule, has a characteristic motor function.[8] They found that the characteristic deglutition pressure complex observed in the upper esophagus was not propagated into the vestibule. There was an absence of the initial negative and positive deflections that are observed in the upper esophagus with swallowing liquids. Fyke, Code, and Schlagel have explored the esophagogastric junction in normal persons

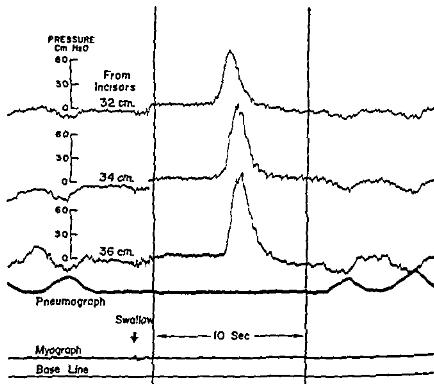


Fig 14 Normal deglutition pressure complexes recorded from lower esophagus Catheter tips are 2 cm apart Myograph indicates onset of deglutition Camera speed 10 mm per second

onset of deglutition It is observed more frequently in the upper than the lower esophagus and is thought to be due to the sudden stretching of the closed esophagus by elevation of the larynx[18,] The negative component is followed by an abrupt increase in pressure of 10 to 15 cm of water Following the abrupt rise in pressure the third component of the complex is observed This consists of a slowly increasing positive pressure change or a plateau of pressure as demonstrated in figures 13 and 14 The fourth and most prominent component of the deglutition pressure pattern is a large simple monophasic positive pressure wave that rises rapidly to a peak and declines with equal speed Thus immediately after deglutition pressure changes

pressure occurs while pressure is increasing in the lower esophagus thus greatly extending the pressure gradient from the lower esophagus to the vestibule The slow decline in pressure is followed by an equally slow increase to form a smooth negative pressure wave This negative pressure wave is continued into a *similar slow positive pressure wave* that appears to occur in sequence with the peristaltic pressure wave of the lower esophagus (fig 15) Below the diaphragm the slow fall and rise of pressure is of less magnitude than when recorded from just above the diaphragm

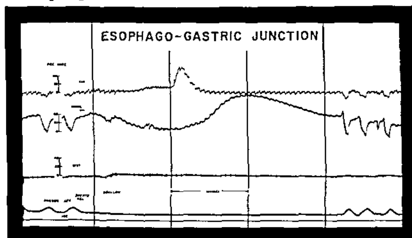


Fig 15 Record obtained from the distal esophagus vestibule and stomach The tip of the middle catheter is recording from the zone of high pressure just above the diaphragm Note the exaggerated respiratory pressure changes with inspiration producing a downward deflection of the light beam indicating the catheter tip is above the diaphragm but still in the high pressure zone The decrease in pressure in the vestibule immediately after the onset of deglutition and the following slow position wave are of greater amplitude than usually observed below the diaphragm The deglution pressure changes were obtained while respiration was stopped Camera speed 10 mm per second (From Hightower N C Jr The physiology of symptoms I Swallowing and esophageal motility *Am J Dig Dis* n s 3 562 1958 Published with the kind permission of the editors of *American Journal of Digestive Disease*)

It appears that the entire vestibule segment serves as a sphincter mechanism that separates the lower esophagus from the stomach [3]

TABLE IV
ESOPHAGEAL PRESSURES

Author	*Site of Recorder*	*Origin of Pressure*		*Mean Pressure*
Hightower[14]	Lower Half	Basal		−5.5 cm H_2O
	Lower Half	Respiration		6.5 cm H_2O
	Lower Half	Cardiovascular		2.4 cm H_2O
Butin *et al* [6]	Mid Esophagus	Primary Wave	Liquid	100 cm H_2O
			Solid	74 cm H_2O
Hightower[33]	Junction Mid and Lower Third	Primary Wave	Liquid	88 cm H_2O
			Solid	72 cm H_2O
Sanchez *et al* [8]	Upper Seven Eighths	Primary Wave	Dry and Solid	40-110 mm Hg
Hightower[14]	Mid Esophagus	Secondary Wave	Balloon	32 cm H_2O
Sanchez *et al* [8]	Ampulla	Primary Wave	Liquid	27 mm Hg†
	Vestibule	Primary Wave	Liquid	5-15 mm Hg

From Hightower, N. C., Jr.: Esophageal motility in health and disease. *Dis Chest* 28:150, 1955.
†One observation only.

with a miniature pressure transducer and encountered a zone of high pressure similar to that encountered at the pharyngo-esophageal junction.[19] This zone of high pressure was found to extend from 1 to 2 cm above the hiatus to 1 to 2 cm below the hiatus and occupies the segment of the esophagus designated as Lerche's gastro-esophageal vestibule. The mean resting pressures in this region are usually 10 to 20 cm of water pressure above atmospheric pressure.[4] Variations in basal pressure in the vestibule due to respiration and cardiovascular pulsations are more marked when recorded from the high pressure zone than any other part of the esophagus.

With deglutition there is an absence of the initial positive component as first pointed out by Sanchez, Kramer and Ingelfinger.[28] Indeed within 1 to 2 seconds after the onset of deglutition the high basal pressure decreases to form a slow negative wave of 7 to 10 seconds duration.[3,19] This decrease in

these patients produces abnormal deglutition pressure pat terns [76, 8] When a pressure gradient does occur it is much less than that observed in the normal esophagus Abnormal pressure waves due to secondary peristalsis are frequently observed When the esophagus becomes completely decompensated there may be no response to deglutition (fig 16)

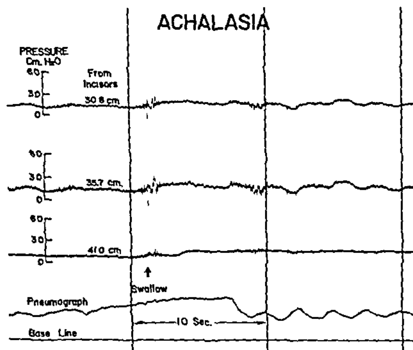


Fig 16 Deglutition response in achalasia. Note positive basal pressure in proximal and middle catheters due to retained liquid and food The distal catheter is in the esophagogastric junctional high pressure zone Complete decompensation has occurred and no deglutition pressure complex is observed in the tracings from the catheters recording from the esophagus nor is there relaxation of the esophagogastric junction Camera speed 10 mm per second

The esophagus in patients with achalasia demonstrates a peculiar sensitivity to Mecholyl® [3, 13] When administered subcutaneously or intramuscularly mecholyl produces a marked sustained

It is now clearly evident that the vestibule exhibits an independent but coordinated motor activity. Normally the vestibule is contracted maintaining the high pressure zone and the deglutition pressure complex recorded from the upper esophagus is not propagated into the vestibule. As the peristaltic pressure wave approaches the vestibule relaxes reflexly, as does the cricopharyngeal muscle at the pharyngo esophageal junction allowing esophageal contents to be emptied into the vestibule by the progressing high pressure gradient between the lower esophagus and vestibular segments. The vestibule then contracts slowly with higher pressures in the part of the segment above the diaphragm than in the lower part below the diaphragm. This provides for emptying the vestibule into the stomach.

Disturbance of Esophageal Motility by Disease Many diseases may alter the normal motor activity of the esophagus. Measurement of intraluminal pressure in patients with dysphagia has increased our understanding of the pathophysiology involved.[30]

Achalasia results in dysphagia due to a disturbance of the normal motor activity of the esophagus.[31] This is manifest mainly by an incomplete propagation of the primary peristaltic wave and the fact that reflex relaxation of the esophageal vestibule does not occur. The primary peristaltic contraction originates in the pharynx in a normal manner but when it has reached the level of the upper esophagus it seems to become ineffective weaker and finally deteriorates and fades away. Secondary peristaltic contractions often occur due to local distention by retained foods and secretion but once initiated these contractions move purposely up or down the esophagus for a short distance then disappear. Without normal propagation of peristaltic contractions little intraluminal pressure gradient is created and esophageal transport is markedly retarded. As the normal motor functions progressively fail the retention of solid foods liquids and secretions occurs which leads to dilatation and elongation of the esophagus.

It has been demonstrated that the primary peristaltic wave in

changes due to spontaneous intermittent contraction of the esophageal musculature may be recorded These rhythmical contractions may occur at a rate of 6 to 12 per minute It has been demonstrated that the sphincteric areas of the esophagus at the pharyngo-esophageal and esophago-gastric junctions respond normally to deglutition

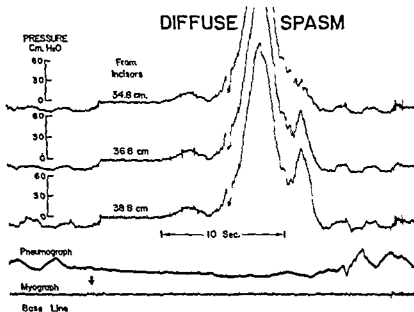


Fig 18 Deglutition response in diffuse spasm Note that the pressure complex occurs simultaneously in all tracings and that they are markedly abnormal in amplitude and duration Camera speed 10 mm per second

Scleroderma is an example of a systemic disease that may produce dysphagia by interference with the third stage of deglutition [77] The primary disorder of esophageal motility is the defective propagation of the primary peristaltic contraction due to a myogenic failure Also there is a rather marked loss of muscular tone in the esophageal wall As in achalasia scleroderma involves most of the esophagus and is not confined to any particular segment although the changes are usually more evident in the lower esophagus

contraction of the esophagus (fig 17) This marked sensitivity to mecholyl is probably due to the defunct intrinsic nerve plexuses for the response obtained following this drug is in keeping with Cannon's law of denervation [34]

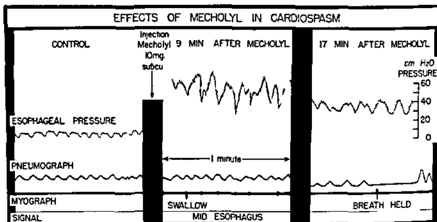


Fig 17 Effects of mecholyl on esophageal intraluminal pressure in achalasia Note the marked rise in intraluminal pressure at 9 and 17 minutes after subcutaneous administration of 10 mg of mecholyl (From Hightower N C Jr Olsen A M and Moersch H J A comparison of the effects of acetyl betamethyl choline chloride (Mecholyl) on esophageal intraluminal pressure in normal persons and patients with cardiospasm *Gastroenterology* *26* 592 1954 Published with kind permission of the editor of *Gastroenterology*)

Diffuse spasm produces dysphagia also as a result of disturbed normal motor mechanisms Dysphagia associated with this disorder characteristically occurs intermittently and is associated with pain *In this disease the esophageal musculature appears* to be hypersensitive to the stimuli produced by deglutition and also by local distention Measurements of deglutition pressure complexes in this disease have revealed that a number of responses may be obtained Following deglutition the deglutition pressure complex may be markedly abnormal in that it is greatly increased in amplitude (up to 300 cm of water pressure) and duration (fig 18) It is noted that contractions may occur simultaneously over a considerable length of the esophagus and be recorded at the same time from all three catheter tips Also immediately following a deglutition pressure complex rhythmical pressure

Moersch Code and Olsen have recently described a motor dis order of the esophagus which exhibits features of both achalasia and diffuse spasm and have used the term *dyschalasia* to designate

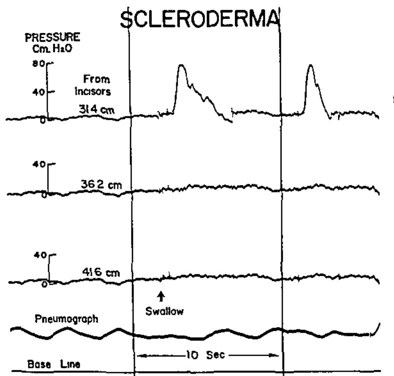


Fig 19 Deglutition response in lower esophagus and esophagogastric junctions recorded from patient with scleroderma Note slightly positive basal pressure in lower esophagus as recorded by proximal and middle catheters The distal catheter is recording from the esophagogastric junction and demonstrates low junctional pressure An abnormal deglutition complex is observed in the upper tracing followed by a spontaneous contraction The complex is not propagated to the tip of the middle catheter and there is no evidence of relaxation at the esophagogastric junction Camera speed 10 mm per second

the disorder [36] Mechanical obstruction produces dysphagia and may result from intrinsic or extrinsic lesions In general condi tions causing mechanical obstruction produce similar disturbances

The primary peristaltic contraction originates normally in the pharynx and passes on into the esophagus but the contraction fades out usually in the upper levels of the esophagus Few deglutition pressure complexes reach the lower esophagus and those that do are usually of low amplitude Apparently the esophagogastric junction is also involved in this disease as we have frequently observed that the high pressure zone at the esophagogastric junction is usually markedly reduced (fig 19) This finding is in keeping with the clinical observation that regurgitation frequently occurs in these patients and that liquids taken in the upright position usually flow unimpeded through the esophagogastric junction Mecholyl® does not increase esophageal intraluminal pressure in patients with scleroderma as is observed in patients with achalasia [33]

Hiatus hernia is a common disorder that may produce dysphagia by anatomical alterations of the normal esophagogastric junction In these patients the high pressure zone of the esophagogastric junction may be found completely above the hiatus The displacement of the esophagogastric high pressure zone upwards and herniation of part of the stomach into the thoracic cavity decreases the esophagogastric pressure gradient and often allows reflux to occur Some degree of peptic esophagitis is not at all uncommon and this probably accounts for the increased irritability and spontaneous contractions frequently observed in pressure recordings This is particularly seen in the lower esophagus where spontaneous contractions may follow a normal deglutition complex or may be induced by manipulations of the catheters Texter and associates have demonstrated that the deglutition complex recorded from the terminal esophagus in patients with hiatal hernia is of low amplitude and prolonged duration [9]

Many other disorders may result in dysphagia and disturbed function of the esophagogastric junction *Chalasia* is a term applied to a relaxed esophagogastric junction that permits esophageal reflux This condition is usually seen in infants but may occur in adults Chalasia is apparently a disorder of the vestibule and occurs because the vestibule does not remain tonically closed as occurs normally [3]

mically and recorded from the antrum their rate is constant at 3 per minute These waves coincide exactly with the "20 second rhythm" described years ago by Carlson [39]

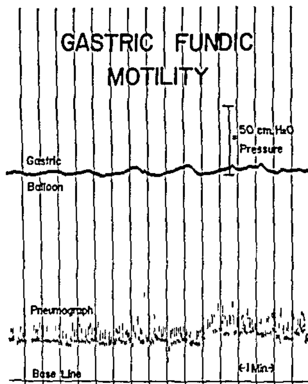


Fig 20 Type I gastric contractions recorded from the fundus of the stomach These contractions are of low amplitude and may occur rhythmically at a rate of approximately 2 per minute Camera speed 0 4 mm per second

It is felt that the type I waves in both the fundus and the antrum represent "mixing" type of motor activity One gets the impression from balloon kymographic records and also from fluoroscopic observations that the slow rise and fall of pressure recorded from the fundus represents a kneading of the gastric contents

in motility. The primary peristaltic contraction may be observed fluoroscopically to skip over the lesion if located in the upper or mid esophagus. When the obstruction exists in the lower esophagus the peristaltic wave progresses to the site of the obstruction without interruption but may be shallow and not strong enough to force barium past the stenosis.[3] As most obstructive lesions occur in the lower esophagus, retention of secretions and swallowed material is not unusual. The resulting distention acts as a stimulus for secondary peristaltic contractions and these waves frequently are observed.

It is recognized that a number of *functional disorders* may result in dysphagia.[8] Detailed observations of the types of motor disturbances in so called functional dysphagia are not available.

GASTRIC MOTILITY

In addition to serving as a temporary reservoir for ingested food and drink, the stomach is provided with certain motor activities to perform mixing of the gastric contents with the products of gastric secretion and to effect gastric evacuation into the small bowel. The stomach is a remarkable organ in that it is capable of greatly increasing its volume without increasing intraluminal pressure. Following an ordinary mixed meal gastric evacuation is usually complete after two hours.

Types of Gastric Motility. When the balloon method of recording motility is used three types of gastric motor activity are recognized on the kymographic film.

Type I waves are of low amplitude and their duration varies depending upon whether being recorded from the fundus or the antrum of the stomach. In the fundus of the stomach these waves are usually less than 10 cm. of water pressure in amplitude and duration varies from 30 to 50 seconds (fig. 20). In the antrum of the stomach the amplitude of the waves are usually 5 cm. of water or less and their duration is from 18 to 22 seconds (fig. 21). They appear as smooth symmetrical humps on the record with respiratory pressure changes superimposed. They occur in both rhythmic and non rhythmic patterns. When present rhyth

the end of a period of activity and is usually followed by quiescence. Type III complexes occur infrequently.

Analysis of Gastric Motility Records. A quantitative analysis of gastric motility records has revealed that the stomach exhibits some type of motor activity approximately 40 per cent of the time when recorded after an overnight fast[9] (Table V). In the gastric antrum type I waves occur 23 per cent of the time of observation, type II waves 15 per cent of the time, and type III waves 1 per cent. A little over half of the type I activity will be of the rhythmical pattern type. About one-third of the type II waves will occur in a rhythmical pattern.

Alterations of Gastric Motility. A number of factors may alter gastric motility. *Disease* of the stomach or of the gastro-intestinal

TABLE V

QUANTITATIVE ANALYSIS OF GASTRIC MOTILITY RECORDS OF TWENTY-FIVE PERIODS OF OBSERVATION OF ONE TO TWO HOURS ON NORMAL HUMAN BEINGS

Type of Motility	Value	Nonrhythmic: Time Per Cent	No. Per Hr	Mean P† cm Water	Mean D‡ Sec	Time Per Cent	Rhythmic: No. Per Min	Mean P† cm Water	Mean D‡ Sec	Total Per Cent Time Present
Type I	Mean	10	23	5	19	13	2.9	5	21	23
	SD	4	22		2	17	0.1		1	17
	SEm±	0.9	4.5		0.3	3.3	0.03		0.2	3.4
Type II	Mean	10	28	22	14	5	3.0	29	12	15
	SD	7	16	8	4	9	0.2	19	2	12
	SEm±	1.5	3.3	1.5	0.8	1.8	0.06	5.4	0.6	2.4
Type III	Mean	1	2	7	§2					
	SD	2	2	2	2					
	SEm±	0.5	0.8	0.9	1.0					
Types I, II and III	Mean									38
	SD									15
	SEm±									3.1

From Hightower, N. C., Jr., and Code, C. F.: The qualitative analysis of central gastric motility records in normal human beings with a study of the effects of neostigmine. *Proc. Staff Meet. Mayo Clin.* 25:697, 1950.

†P = pressure

‡D = duration

§Duration of type III expressed in minutes.

Type II waves are also simple monophasic waves but are of greater amplitude than type I Their rise and decline of pressure is rapid producing a sharp peak Their duration is variable when occurring in a non rhythmic pattern and ranges from 12 to 25 seconds When occurring in a rhythmical fashion however their rate is exactly the same as the rhythmical type I waves—i e 3 per minute[9] (fig 21) Pressure changes produced by these waves and recorded from the balloon usually ranged from 10 to 50 cm of water although at times 100 cm have been encountered The type II gastric contraction represents peristalsis In the antrum this type of motor activity creates the pressure gradient that effects gastric evacuation into the duodenum

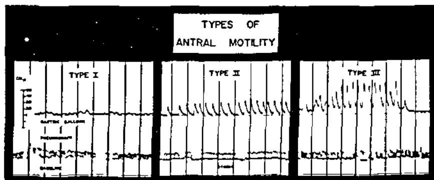


Fig 21 Types of motor activity recorded from the antrum of the stomach Note that the rhythmical rate of the type I and type II waves is approximately 3 per minute Camera speed 0 4 mm per second

Type III waves are complex They consist of two components—one is *a smooth rise and decline of the basal pressure* and the other is type I or type II waves frequently occurring in a rhythmic pattern superimposed upon the change in basal pressure The change in basal pressure is termed the type III wave (fig 21) From a functional standpoint this type of motor activity is thought to represent a change in tonus or alteration of the diameter of the lumen Those tonus changes usually amount of 10 cm of water or less and their duration may vary from 1 to 5 minutes This type of motor activity is most often observed at

Surgical procedures may markedly alter gastric motility Vagotomy produces significant changes in gastric motor activity The primary effects of vagotomy as observed in records of antral gastric motility is a reduction in the incidence of type II waves and consequently a reduction in total activity[11] Although vagotomy produced rather characteristic changes in antral gastric motility sympathectomy has been found to have little effect on the motor activity of the gastric antrum[10]

Drugs of many types may affect gastric motility Today there are many potent anticholinergic agents that are capable of reducing gastric motility The quarternary amines are the most potent type of anticholinergic agent available today[13 40] Drugs of this type produce effects similar to that of vagotomy (fig 22) A quantitative analysis of records obtained from patients with duodenal ulcer who had been given Banthine® revealed that the principal effect was a reduction in type II activity and a consequent reduction in total activity as is observed in vagotomy[13] Parasympathomimetic agents as neostigmine and urecholine apparently have little effect on the normal stomach[41] whereas after vagotomy such a drug may restore gastric motility temporarily to normal[11]

The effects of *smoking* on gastric motility have been studied in our laboratory and we have found that smoking a cigarette produces an inhibition of type II waves This has been observed in normal individuals as well as patients with active duodenal ulcer

SMALL BOWEL MOTILITY

Most of our digestive processes occur in the small bowel It would seem logical then that the types of motor activity observed in the small bowel would aid these digestive processes In general three types of motor activity occur in the small bowel As in the stomach these types of motor activity may be divided into mixing and propulsive[4 44]

Types of Small Bowel Motility From the upper small bowel recordings obtained with either the balloon method or direct pressure measuring method demonstrate two types of waves

tract however has been found to alter gastric motility only slightly An analysis of records of antral motility obtained from 12 patients who had an unobstructed duodenal ulcer revealed that total activity was about the same as that observed in normal individuals There was a qualitative difference however in that the incidence of type II waves was increased with a corresponding decrease in type I waves [10] A similar qualitative deviation from normal was observed in a small group of 7 patients with severe hypertension who were studied prior to thoracolumbar sympathectomy [10]

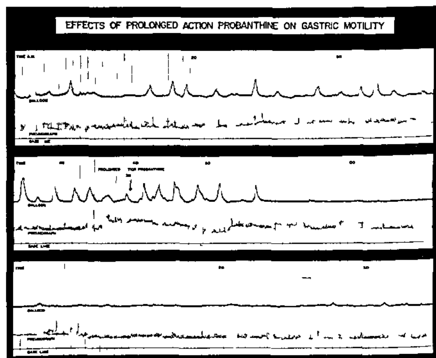


Fig 22 Example of the effect of a potent anticholinergic agent on gastric motility The three panels represent a continuous tracing Note that 9 minutes after 30 mg of the drug is given orally type II contractions were inhibited throughout the remaining period of observation (From High tower N C Jr and Broders A C Jr A new anticholinergic agent in the treatment of peptic ulcer *Tex State J Med* 54 83 1958 Published with kind permission of the editor of *Texas State Journal of Medicine*)

upper jejunum the rhythmical rate of these type I waves is 11 per minute (fig 23) In the terminal ileum the rhythmical rate is 8 per minute (fig 24) Thus in the small bowel of man there is a decreasing gradient from the upper to the lower small bowel of the rate of rhythmical type I waves A similar gradient of rhythmical type I waves was demonstrated in the rabbit years ago by Alvarez[4] and in the dog by Douglas and Mann [46]

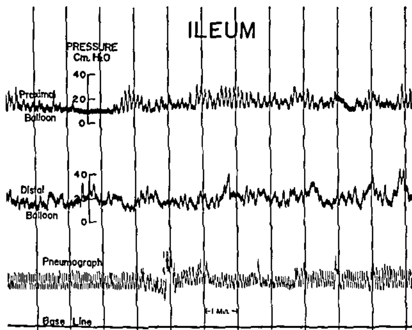


Fig 24 Tracing obtained from lower ileum in patient with iliac stoma Tandem system of balloon used Note rhythmical rate of type I waves is 8 per minute Type III waves are also recorded Camera speed 0 4 mm per second

The amplitude of the type I waves in the small bowel usually represents a pressure of 5 to 15 cm of water The duration of these waves vary from 2 5 to 7 5 seconds [14 47] Type I waves are the most common type of motor activity observed in both the upper and lower small bowel The type I wave recorded from the small bowel is considered to represent a predominantly seg

These are type I and type III From the lower small bowel type I type III and type IV waves are recorded Classical type II waves as observed in the stomach and in the colon have not been recorded from the small bowel with the techniques we have used

Type I waves in both the upper and the lower small bowel are simple monophasic positive pressure waves When occurring in a rhythmic pattern the rate of occurrence of type I waves is extremely constant and characteristic of the segment of small bowel from which the record is obtained In the duodenum and

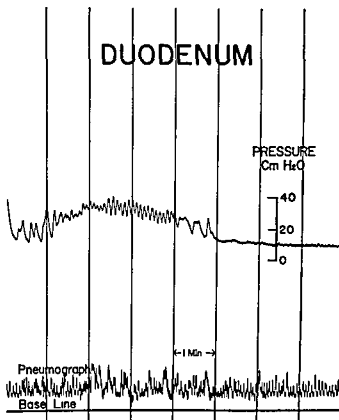


Fig 23 Tracing of motility obtained from duodenum with balloon method of recording Rhythmical type I waves occurring at rate of 11 per minute Note prolonged elevation of basal pressure Camera speed 0 4 mm per second

activity in the upper small bowel is the same as type I activity or about 60 per cent of the period of observation In the lower small bowel type III waves are present 30 to 50 per cent of the time Type IV waves are usually present 5 to 10 per cent of the time

Alterations of Small Bowel Motility The motor activity of the small bowel is subject to alteration by a great many factors other than disease states and pharmacological agents For instance it has been demonstrated that total motor activity of the small bowel may be decreased as much as 30 per cent by the administration of *placebos*[49] It has also been demonstrated that *sleep* produces a marked reduction in motor activity of the small bowel[50] The effect of *nausea* on upper small bowel motility also has been studied[51, 52] What has been observed most often during nausea is a prolonged type III contraction in the upper small bowel with rhythmical type I waves superimposed It should be pointed out however that this type of motor activity has been recorded from normal individuals who were not experiencing nausea and from subjects who had been given morphine[3]

In patients with the *sprue syndrome* it has been found that the amplitude of type I and type III contractions is reduced and that propulsive activity is definitely less than occurs in the normal[4, 4] These observations correlate well with the fact that the transit time of a barium meal through the small intestine of patients with sprue is prolonged[5–7] It is also of interest that transit time is delayed in patients who have *acute dysentery*[58]

Many *pharmacological agents* are capable of altering the motor activity of the small bowel Atropine and tincture of belladonna given orally have been shown to inhibit the motility of the small bowel They produce a reduction in total activity and in the incidence of propulsive type III waves[9] Anticholinergic agents of the quarternary amine type are also potent inhibitors of small bowel motility[44, 60] Tertiary amine compounds of the so-called antispasmodic types usually have little effect on the small bowel motility[61, 6]

mental or mixing type of motor activity This type of motor activity probably serves to bring the intraluminal contents into contact with a larger surface of the bowel mucosa

Type III waves are complex in that they are made up of two components There is an increase in the basal pressure upon which is superimposed type I waves frequently in a rhythmical pattern The duration of the type III waves varies from about one half to 5 minutes and their amplitude ranges from 10 to 40 cm of water as demonstrated in figures 23 and 24 The type III wave is considered to have a propulsive or peristaltic function in the upper small bowel of man

Type IV waves are usually complex This type of wave is observed in the lower small bowel of man [44] It is a propulsive type of motor activity These waves may resemble the type III wave in the upper small bowel in that they may begin with a rise in basal pressure with type I waves superimposed They differ however in that a large positive pressure wave develops that obliterates the type I activity When a tandem system of balloons is used for recording the type IV waves usually register on both balloons in a coordinated manner characteristic of propulsive activity Indeed when recording from the lower ileum in patients with an ileac stoma this type of motor activity is associated with the expulsion of fecal material from the stoma The amplitude of the type IV wave usually varies from 30 to 50 cm of water and the duration of these waves is approximately one and one half minutes

Analysis of Small Bowel Motility Records Analysis of motility records obtained from fasted individuals without disease of the small bowel shows that type I or segmental motility is present approximately 60 per cent of the period of observation in the upper small bowel[48] and about 85 per cent in the lower small bowel [44] In the upper small bowel type III waves are observed about 35 per cent of the time of the period of observation The per cent of time type III waves are present is included under the per cent of time type I waves are present for type I waves are always superimposed upon type III activity Thus total

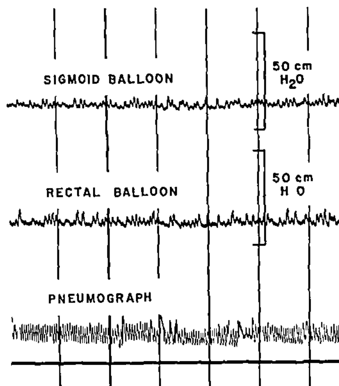


Fig 25 Record of sigmoidal and rectal motility obtained from normal individual Short bursts of rhythmical Type I waves are observed with rate of 11 per minute Camera speed 0 4 mm per second Distance between vertical lines is one minute

Type II waves are similar to the type I They are however of much greater amplitude and of longer duration These waves are usually 25 to 30 seconds in duration and the amplitude usually varies from 15 to 10 cm of water pressure (fig 26) This type of activity accounts for the major portion of total activity seen in records obtained from the colon They sometimes occur in a rhythmical pattern with a rate of about 2 waves per minute The type II waves are caused by the contractions in the large bowel that produced the haustra seen by the radiologist [67] and as observed through a paper thin abdominal wall [43] It is felt that type II waves represent predominantly a mixing

Cholinergic agents as neostigmine and urecholine are effective stimulators of small bowel motility.[63,64] It has been demonstrated that urecholine increases the transit time of a barium meal through the small bowel[67] and neostigmine increases the incidence and amplitude of propulsive type III contractions.[63]

Morphine exerts a unique action on the motor activity of the small bowel. It markedly increases the tone of the bowel. The incidence of non propulsive type I waves is increased.[44] However, there is a marked decrease in the propulsive type III contractions.[44,53,65,66] This probably accounts for the constipating effect of morphine.

COLONIC AND RECTAL MOTILITY

The colon serves as a reservoir for the contents emptied into it from the small bowel. There is considerable absorption of water and electrolytes from the contents of the colon and much of the motility of this organ is devoted to a mixing type of action. Peristalsis in the true sense as occurs in the small bowel is not observed in the colon. Propulsive motility does occur, however, but this is usually in the form of a mass movement activity.

Types of Colonic and Rectal Motility. Four types of motility waves are recorded from the colon with balloon and direct pressure measuring systems.

Type I waves are small simple monophasic positive pressure waves of low amplitude and short duration and similar to the same type of wave occurring in other parts of the alimentary canal (fig. 25). The exact function of the type I wave is not known but presumably it serves as a component of motor activity which contributes to mixing of the intestinal contents. The amplitude of type I wave is usually 5 to 10 cm of water pressure and the duration varies from 5 to 10 seconds. When occurring in a rhythmic pattern the rate varies from about 8 to 12 per minute depending upon the site from which they are recorded. Type I waves frequently occur as part of the type III complex.

Type IV waves Type IV wave results from the "mass move ment activity of the colon and rectum These waves are rarely recorded from a normal individual These waves rarely occur in a rhythmical pattern except in patients with chronic ulcer ative colitis and then the rate is usually about 1 wave every 2 to 3 minutes The amplitude of the type IV may reach 80

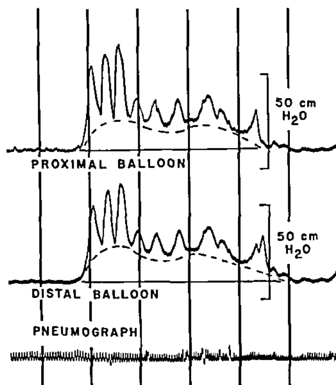


Fig 27 Record from descending colon via colonic stoma Note rise in basal pressure with superimposed type II waves Note that both balloons are recording the type III complex indicating that it extends over a seg ment of colon at least 7 cm in length Camera speed and time lines are the same as in figure 25

to 100 cm of water pressure The duration of the waves is characteristically prolonged and lasts from 2 to 4 minutes Their configuration is rather characteristic in that there is a rather

type motor activity although they may contribute to some extent to propulsion [4]

Type III waves are a complex pattern of an increase in basal pressure or a change in tonus on which is superimposed type I or type II waves or both These waves usually last from 1 to 4 minutes and the pressure change in baseline tonus is usually

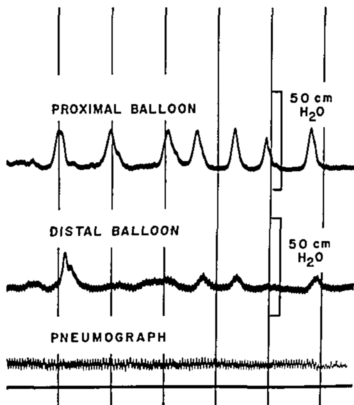


Fig 26 Record obtained from transverse colon via colonic stoma Classical type II contractions Note contractions occurring in proximal balloon are only 7 cm proximal to lower balloon Camera speed and time lines are the same as in figure 25

less than 10 cm of water (fig 27) The exact function of the type III wave is not clear but is probably predominantly mixing in its action

observation and type III waves 2 to 4 per cent Type IV waves are rarely observed normally and are present less than 1 per cent of the period of observation

Alterations of Colonic and Rectal Motility There are many factors which may alter colonic and rectal motility The effects of *emotions* on colonic motility has been extensively studied [68-73] It has been found that pain increases the contractions of the colon in normal subjects Discussion of life situations that pro duced emotional conflict resulting in feelings of anger anxiety apprehension resentment hostility or guilt caused increased motor activity However when fear fright or dejection were the predominant feeling of the subject hypomotility resulted The type of motor activity recorded in patients with *chronic ulcerative colitis* is rather characteristic [1 74] Records obtained from these patients show a marked increase in the incidence of type IV waves associated with propulsive action leading to expul sion of the balloons or fecal matter Type I activity is increased and there is a significant decrease in type II activity and a com plete lack of type III waves in patients with ulcerative colitis Thus total motor activity is decreased in these patients due mainly to a reduction in the mixing type of motor activity At the same time propulsive motility is increased

Many drugs may influence the motor activity of the colon *Anticholinergic* agents of the quarternary amine type are potent inhibitors of colonic motility [61 75 76] *Parasympathomimetic agents* as neostigmine and Mecholyl® stimulate colonic motility Neostigmine is particularly effective in producing a predom inantly propulsive type of motor response [77] *Morphine* increases the amount of non propulsive motility and tends to eliminate propulsive activity Morphine also markedly increases the tone of the large bowel [43] Most of the so called *antispasmodic and spasmolytic agents* when administered by mouth in the recom mended therapeutic doses have little or no effect on motility of the large bowel

rapid increase in pressure at the beginning of the wave the peak is reached and then there is a rapid decline for 50 to 60 per cent of the elevation Then the rate of decline changes and becomes much slower producing a prolonged wave (fig 28)

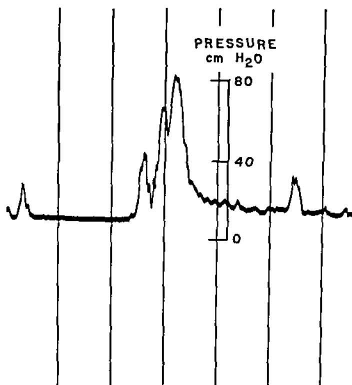


Fig 28 Type IV contraction recorded from sigmoid colon of patient with chronic ulcerative colitis Note pressure exceeds 80 cm water A type II contraction is observed at each end of tracing Camera speed and time lines are the same as in figure 25

Analysis of Colonic and Rectal Motility Records Some type of motor activity is recorded from the colon and rectum 35 to 40 per cent of the period of observation when the individual has fasted overnight [17] The predominant activity is the *type II* wave and accounts for 90 to 95 per cent of total activity Type I waves usually occur during 1 to 2 per cent of the period of

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cular contractions in several areas and finally the effect of these contractions on the movements of the intraluminal contents However with existing methods and equipment this is not possible in man Detection and recording of intraluminal pressures has a number of advantages as a means of studying gastrointestinal motor activity The pressure data are objective quantitative and comparable to that obtained in other laboratories and seem accurately to reflect the muscular activity of the wall adjacent to the point of recording In order to record intraluminal gastrointestinal pressures tubes or wires have been passed through the nose mouth and anus Esophageal and gastric pressures are satisfactorily recorded by this means but small intestinal and colonic records are more difficult to obtain The long small bore tubes usually required to transmit pressures from the distal small intestine and proximal colon to external manometers may result in an inadequate frequency response The tubes often cause the patient considerable discomfort and this may limit the length of the recording period as well as affect the motility under study

The desirability of recording motility without tubes led us several years ago to record and quantitate borborygmi by means of an abdominal microphone [1] Unfortunately localization of the origin of the sounds to particular areas of the intestines was not possible

In early 1956 we discussed the feasibility of tubeless intraluminal pressure recordings with Dr Vladimir Zworykin of the Rockefeller Institute for Medical Research and the Radio Corporation of America Dr Zworykin and his colleagues designed and built a pressure sensitive radiotelemetering capsule which permits permanent recording of gastrointestinal intraluminal pressures without the necessity of intubation Prior to completion of this device a most interesting development was reported from the Department of Psychology of the University of California in Los Angeles [3] Drs Wenger Henderson and Dinning recorded the movements within the stomach of a tiny tubeless intraluminal magnet This was accomplished by an external magnetometer which translates movement of the capsule into electric variations Another tubeless method was a

STUDY OF GASTROINTESTINAL MOTILITY BY A RADIOTELEMETERING CAPSULE

JOHN T FARRAR M D *

GASTROINTESTINAL motility may be studied in a variety of ways The principle methods used in man are shown in figure 1 No single one of these will yield information on all

SPECIFIC METHODS OF MEASURING MOTILITY

- ROENTGENOGRAPHY
- LARGE BALLOONS
- PRESSURE MEASURING DEVICES
  - Open Tip Catheters and Rigid Sensitive Manometers
    - Fluid filled catheters
    - Air filled catheters
  - Small Balloons and Rigid Sensitive Manometers
  - Intraluminal Electric Transducers
    - Gauer transformer
    - Radiotelemetering capsule
- DIRECT OBSERVATION
- ABDOMINAL SOUNDS
- ELECTROMYOGRAPHY

Fig 1 Methods of studying the motility of the gastrointestinal tract in man

parameters of motility Ideally we should like to record simultaneously the efferent nerve impulses to the smooth muscles the mechanical and electrical manifestations of intestinal mus

* Assistant Professor of Clinical Medicine Cornell University Medical College New York and Chief Gastroenterology Section Veterans Administration Hospital New York
Supported in part by a grant from Sandoz Pharmaceuticals Division of Sandoz Inc

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radiotelemetering capsule quite similar to the one we are using which was developed independently and approximately simultaneously at the Karolinska Institute in Sweden [4]

This paper is devoted to a description of the radiotelemetering capsule and its use in the gastrointestinal tract We have previously reported some portions of this work [5] The newer phases have been carried out in cooperation with Drs Lawrence Horowitz and Arthur Berman

METHODS

The instrument we have used is a rigid cylindrical plastic capsule 3 0 cm in length and 1 0 cm in diameter (figure 2)

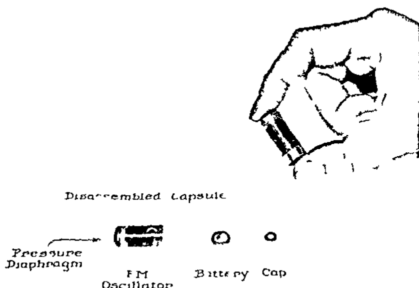


Fig. 2 Radiotelemetering capsule From Farrar and Bernstein (5) Reproduced by kind permission of the author and the Editor of *Gastroenterology*

A pressure transducer comprising a flexible diaphragm and a variable reluctance magnetic circuit frequency modulates a transistor oscillator in response to pressure variations (figure 3) Electromagnetic coupling between this magnet circuit and an

antenna communicates the signal to a frequency modulation receiver The output of the receiver is amplified and the pressure fluctuations recorded oscilloscopically and permanently on paper The distance of the capsule to the antenna does not affect the amplitude of the recorded pressures as long as this distance is not greater than 3 feet Power for the oscillator is supplied by a 1 2 volt rechargeable cadmium cell which has a life of approximately 24 to 30 hours The capsule responds linearly to pressures up to approximately 120 cm of H O and

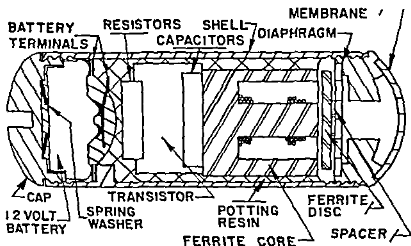


Fig 3 Cross sectional diagram of the radiotelemetering capsule From Farrar Zworykin and Baum (2) Reproduced by kind permission of the authors and the Editor of *Science*

to frequencies from 0 to 100 cycles per second In order to protect the transducer from the effect of contact with gastro intestinal fluids the capsule is covered by a flaccid loosely fitting dipped natural rubber sac 0025 inch in thickness made especially for us and kindly supplied by Julius Schmid Inc of New York Prior to each motility study the capsule and the f m receiver and recorder are calibrated by means of a simple water manometer This calibration permits derivation of accurate relative intraluminal pressures from the final record

Since anatomic or functional narrowing may prevent passage

of the capsule all patients have roentgenographic studies to rule out such obstructing lesions before the study The capsule is swallowed without difficulty by most patients and passes through the entire gastrointestinal tract without causing any physical discomfort or other subjective sensation Since the capsule is radiopaque (figure 10) it may be localized by fluoroscopy or roentgenography During the motility test the patient may lie on a padded fluoroscopy table or sit in a chair For certain studies we have found it desirable for the patient not to be in the same room with the fluoroscope and recording device since this electronic equipment appears to cause some mild apprehension The signals transmitted by the capsule are picked up by a single loop antenna which rests on the abdomen Respirations are recorded simultaneously by an inflated balloon placed under the patient's belt and connected to a strain gage manometer Since the capsule is oscillating constantly during the 24 hour "life" of the battery the pressure tracings may be observed on the oscilloscope for long periods and permanent records made whenever desired In the initial studies long delays occurred after ingestion before the capsule passed into the duodenum This rendered small intestinal and colonic studies inconvenient on the day the capsule was ingested The usual procedure at present for small intestinal pressure studies is for the patient to swallow the capsule the night before A piece of surgical thread 60 90 cm in length is attached to the capsule anchored externally and prevents the capsule from passing beyond the distal duodenum during the night On the day of the study recordings may be made with the capsule held stationary or the string may be cut and recordings made with the capsule free to move downstream For purposes of recording colonic pressures the capsule is also ingested the evening before the study but the anchoring thread is omitted On the morning of the study the capsule is usually in the cecum though occasionally in the distal ileum This permits maximum flexibility in recording during most of the day Upon completion of the study all stools are saved until the capsule is recovered The capsule is easily found and extracted from the stool

RESULTS

A capsule has been taken orally 52 times by 44 patients These include normal controls post gastrectomy patients those with *functional complaints and no organic disease one patient with* the malignant carcinoid syndrome and one patient with unsuspected carcinoma of the sigmoid colon

The total transit time of an object through the gastrointestinal tract provides information on propulsive motility An unusually long or short passage time would suggest that either the object was handled differently from other substances or that it evoked *an abnormal motor response With the exception of the two* patients with tumors the capsule traversed the gastrointestinal tract in an average of approximately 40-48 hours with a range of 1-4 days This corresponds closely to the transit times reported with marker substances and food residues [9]

Intraluminal esophageal pressures have been recorded in one normal subject and a portion of the record is shown in figure 4

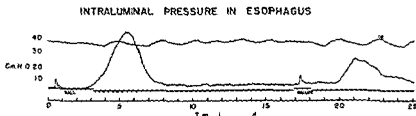


Fig 4 Intraluminal pressures recorded from the mid esophagus The capsule was held in place by a thread

The pressure fluctuations following a swallow correspond to those observed by means of other methods The stationary capsule has little advantage over existing methods for measuring esophageal pressures and its size makes it unsuitable for use in the vestibular area We have not as yet recorded esophageal pressures while the capsule is being normally propelled down the esophagus

Intragastric pressures have been recorded in 10 patients No attempt has been made carefully to study gastric motor activity or the factors which influence it When waves were observed however they occurred at a rate of approximately three per minute as seen in figure 5 and often attained an amplitude of over 75 cm of H O These waves are quite similar to those previously described as occurring in the stomach [8]

INTRALUMINAL PRESSURE OF STOMACH

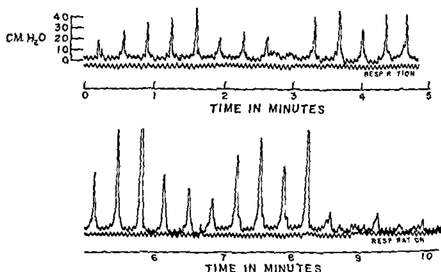


Fig 5 Intraluminal pressure of the stomach From Farrar J T and Bernstein J S Recording of Intraluminal Gastrointestinal Pressures by a Radio telemetering Capsule *Gastroenterology* 35 603 1958 Reproduced by kind permission of the authors and the Editor of *Gastroenterology*

Small intestinal pressures have been recorded in 25 patients The records obtained in normals show considerable variation in the amount of activity present as well as in the amplitude of the waves Great difficulty exists in accurately quantitating these records and in categorizing the individual wave forms However the pressure records are quite similar to those reported by others[7] The most characteristic wave form is the simple type I[8] or segmented wave which may be seen in figure 6 This occasionally occurs with almost absolute periodicity but usually is less regular One patient complained of cramping periumbilical pain while the capsule was recording from the proximal jejunum (fig 6) It is certainly not established that the pain in this patient was originating from the area from which this tracing was recorded However the pain distribution would suggest that the small intestine was the source and it is possible that the active pressure fluctuations seen are associated with the symptoms

INTRALUMINAL PRESSURE OF SMALL INTESTINE

PROXIMAL JEJUNUM OF NORMAL PATIENT



JEJUNUM IN PATIENT WITH PERIUMBILICAL PAIN

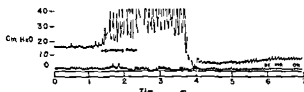


Fig 6 Intraluminal pressure of small intestine in two patients The upper record is from a normal patient The lower record was obtained while patient was complaining of periumbilical pain

INTRALUMINAL PRESSURE OF JEJUNUM IN PATIENT WITH FUNCTIONAL SYMPTOMS AND NO ORGANIC DISEASE

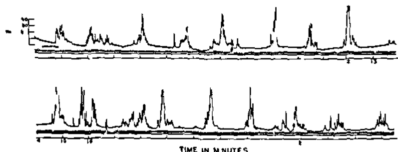


Fig 7 A continuous 28 minute intraluminal pressure record from the jejunum of a patient with functional gastrointestinal complaints and without organic disease Farrar J T and Bernstein J S Recording of Intraluminal Gastrointestinal Pressures by a Radiotelemetering Capsule *Gastroenterology* 3, 603 1958 Reproduced by kind permission of the authors and editor of *Gastroenterology*

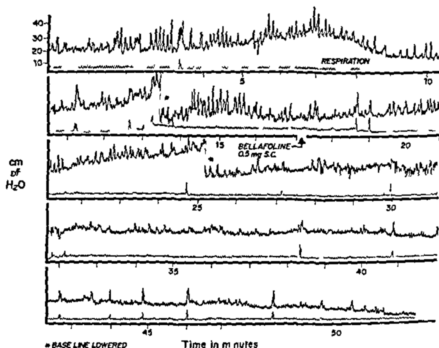


Fig 6 Intraluminal pressure record of distal jejunum before and after parenteral administration of an anticholinergic agent (Bellafoline®)

In several patients with functional gastrointestinal complaints and no organic disease we have observed pressure records which are quite different from those seen in normals An example of this is shown in figure 7 The periods of inactivity alternate fairly regularly with bursts of activity Further study is necessary to establish the consistency and possible specificity of this pattern in patients with functional gastrointestinal disease

The telemetering capsule may be used to evaluate the effect of certain pharmacologic agents on gastrointestinal motility In figure 8 is seen a small intestinal pressure record before and after the subcutaneous injection of Bellafoline® a potent anticholinergic Definite inhibition of activity occurred

Intraluminal colonic pressures have been recorded in 13 patients The patterns are quite variable waves usually occur at irregular intervals and occasionally in rhythmic sequence at rates varying from one to 7 per minute Insufficient data are available at present to characterize adequately the normal trac

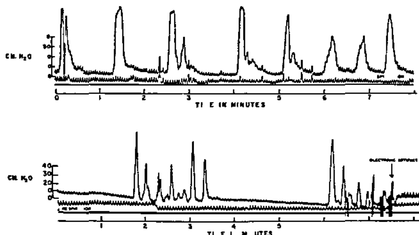


Fig 9 Intraluminal pressure records in the right colon The upper tracing was recorded in a patient diagnosed as having the irritable colon syndrome The lower tracing was recorded as an asymptomatic patient Reproduced by kind permission of the authors and the editor of *Gastroenterology*

ings in the right and left portions of the colon The record in one patient with an irritable colon syndrome is shown in figure 9 The waves resemble those noted in the distal colon in patients with ulcerative colitis [9, 10] In an attempt to relate colonic motor patterns with propulsion of intraluminal contents we are performing serial x ray studies to localize the capsule Figure 10 shows colonic pressures recorded while the capsule was being propelled distally

DISCUSSION

These studies indicate that satisfactory intraluminal pressure records can be obtained by means of a radiotelemetering capsule The wave forms on the records from the esophagus stomach small intestine and colon have the same general configuration as those recorded by other methods This method however has the following advantages

(1) The *telemetering capsule responds to and transmits with* fidelity all physiologically significant pressure changes within the gastrointestinal tract

(2) Since motility studies carried out with the capsule cause no discomfort to the patient and the capsule does not seem

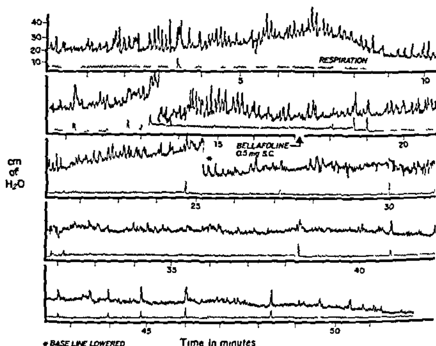


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intermittently downstream rather than recording the pressure fluctuations within a single segment

(2) The 24 to 30 hour life of the battery limits the length of the recording periods Developments are being made to over come this disadvantage

(3) Though the telemetering capsule will pass without difficulty through the normal gastrointestinal tract its passage may be arrested by functional or anatomic narrowing A smaller model is currently being developed

(4) Exact localization of the capsule within the small intestine at frequent intervals is difficult

In addition to the significant information on gastrointestinal motility made available by this method this device demonstrates a technique which may be applicable to the acquisition of other information from within the gut The Swedish group has reported a pH sensitive capsule [11] Other parameters that might be similarly detected and transmitted are temperature radio activity presence of blood electrolytes or other chemical substances Any information which can be expressed electrically may be susceptible to study by this method

SUMMARY

Gastrointestinal motility may be studied by means of an ingestible pressure sensitive radiotelemetering capsule

The capsule has been ingested 52 times by 44 patients and intraluminal pressure records obtained from the esophagus stomach small intestine and colon Because of the ease with which significant data are permanently recorded this method appears to have considerable potential in the study of gastrointestinal physiology

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INTRALUMINAL PRESSURE IN ASCENDING AND TRANSVERSE COLON

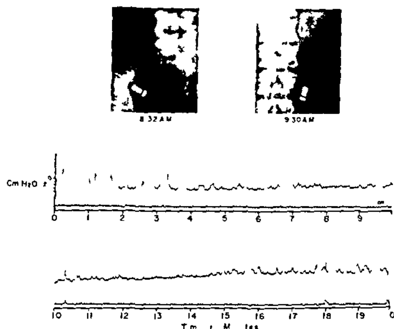


Fig 10 Intraluminal pressures recorded at the time the capsule was moving from the right to the left colon

to elicit an abnormal motor response the method would seem to permit recording of normal motility

(3) It permits for the first time prolonged recordings of the intraluminal pressure of the distal small intestine and proximal colon hitherto almost inaccessible to study

(4) Because of the simplicity of the procedure and the comfort to the patient intraluminal pressure records may be obtained in patients too ill to tolerate other methods

(5) The capsule is radiopaque and moves freely and recording of its movements will provide information on propulsive motility

There are certain limitations or disadvantages of the method using the telemetering capsule

(1) Analysis of the complex wave forms seen on the pressure records may be further complicated when the capsule is moving

THE EFFECTS OF BOWEL FUNCTION ON THE CIRCULATORY SYSTEM*

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SAUL S SAMUELS M D
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INTRODUCTION

THE exertions of stool straining cause serious disturbances in cardiac pulmonary and peripheral circulation which result not

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*This paper was delivered by Alfred Halpern

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mental conditions of the Valsalva maneuver (elevated intra thoracic pressure of 40 mm Hg or greater sustained for at least 8 seconds) It was determined (fig 1) that the Valsalva maneuver was performed during approximately 12 per cent of the straining episodes of normal individuals using a commode The incidence is more than doubled 28 0 per cent by substituting a bedpan for the commode and is increased approximately five fold 57 9 per cent by constipation A constipation corrective* reduces the number of strains exceeding 40 mm Hg and also those exceeding 8 seconds (fig 2)

The Circulatory Response to the Valsalva Maneuver

The circulatory response to the Valsalva maneuver is generally expressed through the changes in blood pressure and heart rate The blood changes occur in four phases[7, 9] (fig 3) Phase I begins with the onset of straining and consists of a brief rise in both systolic and diastolic pressures which is rapidly followed by a precipitous fall Phase II starts at the lowest point and continues until the release of the strain During phase II the arterial pressure begins to rise although the pulse pressure is reduced With the release of the strain (phase III) the systemic blood pressure falls sharply and in phase IV this is succeeded by a marked rise in systolic and diastolic pressures above the control values During the phase IV overshoot a slowing of the pulse rate and an increase in pulse pressure occur before the blood pressure returns to normal

Effect of Straining on the Heart

Effects on the Heart Rate At a blowing pressure of 20 mm Hg expended by normal subjects for 8 to 10 seconds all strains result in an increase in the heart rate during phase II When the duration of the 20 mm Hg pressure strain is reduced to below 8 seconds the number responding with an increased heart rate drops (fig 4)

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* The constipation corrective used was Senokot® the trade name of the Purdue Frederick Company for standardized concentrated active principles of senna pod

infrequently in death[1] Straining at stool which elevates intra thoracic pressure *can precipitate the anginal syndrome*[2-4] More over the changes in blood pressure cardiac output and vaso motor tone during and following stool straining have all been invoked as a cause[5] of myocardial infarction and pulmonary embolism The veins of the legs and pelvis are the sources of 95 to 98 per cent of the freely traveling clots which cause pul monary embolism[6] Although the exact mechanism for mobili zation of these thrombi is unknown it is possible that extreme changes in peripheral vascular caliber as well as modification of arterial and venous pressure may play a significant role in dislodging them

It is the purpose of this presentation to assess quantitative data pertaining to the influence of stool straining during defeca tion on the cardiovascular and peripheral vascular systems of normal and constipated individuals This assessment is based upon our findings after an investigation of the cardiovascular dynamics of bowel function[10] studied by analyzing the magni tude and duration of intrathoracic pressures and the effects of these strains on the heart and arterial blood pressures and the peripheral vascular dynamics of bowel function[20] by determin ing the changes in peripheral venous pressure segmental and digital arterial blood flow and peripheral vascular resistance in order to ascertain their possible influence on thrombus mobili zation

EXPERIMENTAL FINDINGS

The Intrathoracic Pressures of Straining

During straining at stool normal individuals using a commode or a bedpan and constipated individuals using a commode per form the Valsalva maneuver (sustained forced expiration against a closed glottis or other suitable external obstruction to air flow) When compared to normal bowel function on a commode both constipation and the use of a bedpan increase the frequency duration and intensity of strains during single acts of defecation and increase the frequency of exertions initiating the experi

FIGURE 2

Th Eff C C on h M ni ud Du f St ini in th C tipated P t nt

ARTERIAL BLOOD PRESSURE RESPONSE TO THE VALSALVA MANEUVER



FIGURE 3

When the blowing pressure is reduced to 10 mm Hg there is a further marked overall reduction in incidence of heart rate acceleration during phase II When the 10 mm Hg strain pressure is sustained for periods of less than 8 seconds the number responding is reduced still further

During poststraining systolic "overshoot" (phase IV) relative bradycardia occurs in almost all subjects However when mini

DISTRIBUTION OF STRAIN EPISODES ACCORDING TO CRITERIA FOR VALSALVA MANEUVER

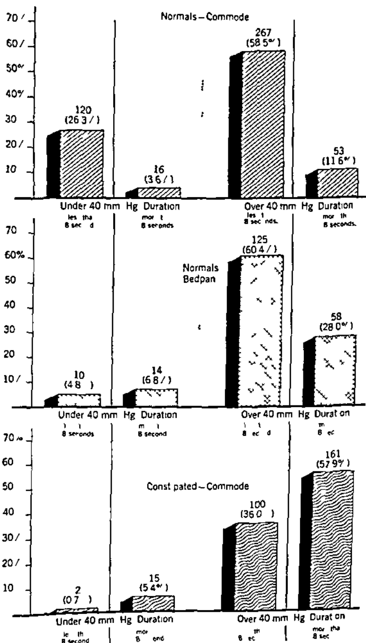


FIGURE 1

mal pressures of 10 or 20 mm Hg are maintained for periods of from 4 to 10 seconds the incidence is markedly lowered. Post strain bradycardia is a characteristic of phase IV of the Valsalva maneuver.[7,10] It is of special interest to note the occurrence of alterations of the heart rate when the conditions do not meet the Valsalva criteria. This suggests that minimal strains may stimulate pressure sensitive centers (e.g., carotid sinus) which are capable of influencing the heart rate independently.

Effect on Circulation Time. The Valsalva maneuver delays the circulation time by an interval approximately equal to the strain period.[11,12] The delay in circulation time closely approximates the duration of strain only within the broader framework of the Valsalva criteria (Table I). Prolongation of circulation time which occurs during shorter periods of strain may be accounted for by the effect of holding the breath.[10]

TABLE I

Increase of Circulation Time with Strains of Differing Magnitudes and Duration*

Intra thoracic Pressure mm Hg	*Strain Duration* 15 sec	10 sec	8 sec	6 sec	4 sec	*Effect of Cumulative Straining for 2 sec* †
60	13.6	9.6	7.8	6.1	3.2	—
40	14.8	10.4	8.1	5.8	2.2	4.3
30	14.3	9.3	8.2	5.6	2.4	2.6
20	12.2	8.4	7.4	4.7	1.1	1.2
10	6.1	4.3	4.2	3.1	‡	1.4

*The values indicated represent the average increase in circulation time in seconds over the control level.

†Each strain was maintained at the indicated level for 2 sec which was repeated five times at 2 sec intervals.

‡Less than 1 sec and probably within the limits of experimental error.

With respect to the delay in circulation time the duration of the strain appears to be of greater significance than the pressure exerted. The similarity of strain duration to delay in circulation time is not as precise for strains of less than 6 seconds regardless of the magnitude of the pressure exerted. Moreover

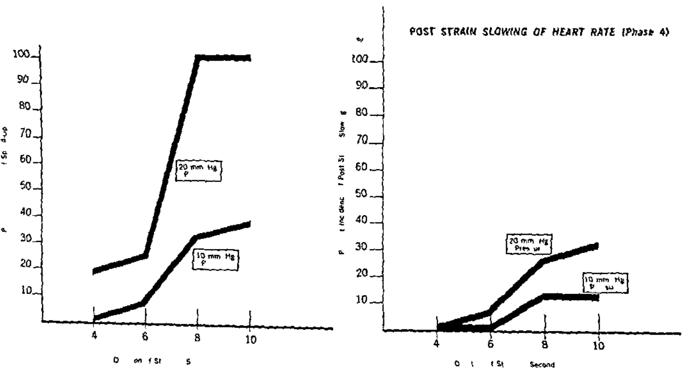


FIGURE 4

The Effect of Straining on the Heart Rate

mal pressures of 10 or 20 mm Hg are maintained for periods of from 4 to 10 seconds the incidence is markedly lowered Post strain bradycardia is a characteristic of phase IV of the Valsalva maneuver [7-10] It is of special interest to note the occurrence of alterations of the heart rate when the conditions do not meet the Valsalva criteria This suggests that minimal strains may stimulate pressure sensitive centers (e g carotid sinus) which are capable of influencing the heart rate independently

Effect on Circulation Time The Valsalva maneuver delays the circulation time by an interval approximately equal to the strain period [11 1] The delay in circulation time closely approximates the duration of strain only within the broader framework of the Valsalva criteria (Table I) Prolongation of circulation time which occurs during shorter periods of strain may be accounted for by the effect of holding the breath [10]

TABLE I

INCREASE OF CIRCULATION TIME WITH STRAIN OF DIFFERING MAGNITUDES AND DURATION

Intra thoracic Pressure mm Hg	*Strain Duration* 15 sec	*10 sec*	*8 sec*	*6 sec*	*4 sec*	*Effect of Cumulative Straining for 2 sec †*
60	13 6	9 6	7 8	6 1	3 2	—
40	14 8	10 4	8 1	5 8	2 2	4 3
30	14 3	9 3	8 2	5 6	2 4	2 6
20	1_2	8 4	7 4	4 7	1 1	1 2
10	6 1	4 3	4 2	3 1	‡	1 4

The values indicated represent the average increase in circulation time in second over the control level

†Each strain was maintained at the indicated level for 2 sec which was repeated five times at 2 sec intervals

‡Less than 1 sec and probably within the limits of experimental error

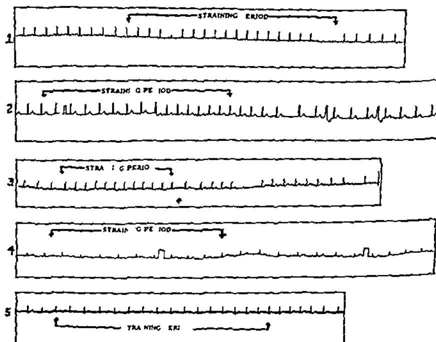
With respect to the delay in circulation time the duration of the strain appears to be of greater significance than the pressure exerted The similarity of strain duration to delay in circulation time is not as precise for strains of less than 6 seconds regardless of the magnitude of the pressure exerted Moreover

there is little or no cumulative effect exerted on circulation time by strains of 2 seconds each

It appears therefore that neither the multiple exertions for short periods of time nor individual strains of less than 6 seconds

FIGURE 5

The Electrocardiographic Changes Observed During the Valsalva Maneuver Associated with Stool Straining



Elect oca d g ph ch nge 1 d 2 p od ed by st g d n g the Val alv m er f I ers on of T w dur ng pe od of st a w th ret l norm l th postste s ng period g D pre n of the ST gme t d i ch d a d n g t a pe od w th occ rence f interpol ted ve tric l t yst les th post t g per od as oc ted w th relat brad c rd a aft train g 3 Depre of th ST s gm t d n g t a g d ppea e f th We k bach phe omenon (2° block) f llow g tr n 4 a d 5 H it g d d appe r f T w es d i g t ng

duration will grossly affect the circulation time However sus tained efforts exerted at pressures in excess of 10 mm Hg for more than 6 or 8 seconds will prolong circulation time in rough approximation to the duration of the strain

Effect on the Electrocardiogram Because a decreased coro nary flow occurs during the Valsalva maneuver straining efforts

during defecation may affect the myocardium. In approximately 20 per cent of the 122 subjects performing the Valsalva maneuver the electrocardiogram revealed four major types of changes: ST depression of at least 0.5 mm, flattening of the T wave, post straining arrhythmia, and reversal of a previously abnormal T wave to one which was flat to upright (fig. 5). These abnormalities are generally associated with physiologic myocardial insufficiency. The time of maximum E.C.G. abnormality was generally between 4 to 8 seconds after the beginning of the strain.

Effect of Straining on Arterial Pressure

An initial rise in blood pressure above 20 mm Hg (phase I) was caused by approximately 83 per cent of the strain episodes of the normal group and by approximately 95 per cent of the strain episodes of the constipated group (Table II). The frequency of pressure peaks between 60 mm Hg and 20 mm Hg was remarkably similar for both groups. At the extremes, however, the constipated series exhibited approximately twice as many systolic pressure responses above 60 mm Hg as the normals, but the normals exhibited approximately three times as many peaks falling below 20 mm Hg as the constipated series. Thus there appears to be a direct relation between the amount of strain and the height of the initial systolic pressure elevation. This is exhibited most strikingly with the greater pressure efforts

TABLE II

QUALITATIVE DISTRIBUTION OF INITIAL SYSTOLIC PRESSURE RISE ON STRAINING DURING BOWEL FUNCTION

Systolic Blood Pressure	*Frequency Distribution*							
	Normals				*Constipated*			
mm Hg	*No*	*%*	*Cum No*	*Cum %*	*no*	*%*	*Cum no*	*Cum %*
Over 60	16	7.2	16	7.2	31	14.2	31	14.2
50–59	45	20.4	61	27.6	51	23.4	82	37.6
40–49	68	30.8	129	58.4	46	21.1	128	58.7
30–39	36	16.3	165	74.7	42	19.3	170	78.0
20–29	19	8.6	184	83.3	36	16.5	206	94.5
Below 20	37	16.7	221	100.0	12	5.5	218	100.0

Phase III of the circulatory response to the Valsalva maneuver begins with the interruption of the strain and is characterized by an abrupt drop in pressure This is followed by an over shoot a marked rise (phase IV) above that of the prestrain levels which was observed in the constipated subjects (fig 6)

FIGURE 6

The Occurrence and Distribution of the Systemic Blood Pressure Over Shoot During Bowel Function

The peak rise in arterial pressure when present occurs within 7 to 10 seconds after the release of the strain and ranges from 20 to 60 mm Hg above the prestrain systolic level There appears

to be no relationship between the degree of initial straining and the height of the post straining blood pressure peaks The almost threefold increase in its incidence among the constipated group as compared with the normals is consistent with the relative frequency of straining efforts meeting Valsalva conditions The blood pressure returns to the prestrain level within 20 to 45 seconds after the release of the strain in all instances

The Effect of Straining on the Peripheral Venous Pressure

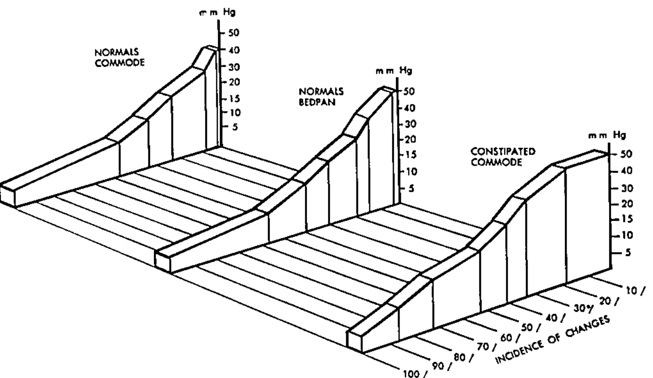
The individuals posture on the commode will influence the stress on the venous system Most individuals support the upper part of the body with the forearms resting upon the knees The pressure of this position plus that exerted by the toilet seat impede venous return This may be significant to the constipated subject who generally requires extended periods of time for defecation

The greater incidence of prolonged and more intense straining episodes during defecation of the constipated group is reflected in the larger number of high venous pressure elevations when compared with the normal group at the commode (figs 7 and 8) This correlation is also apparent when the over all venous pressure profile of the normal group using the bedpan is compared with those normals using the commode

The degree of dependency of the venous system influences the response The less dependent veins of the arm exhibit smaller pressure increases than those in the leg

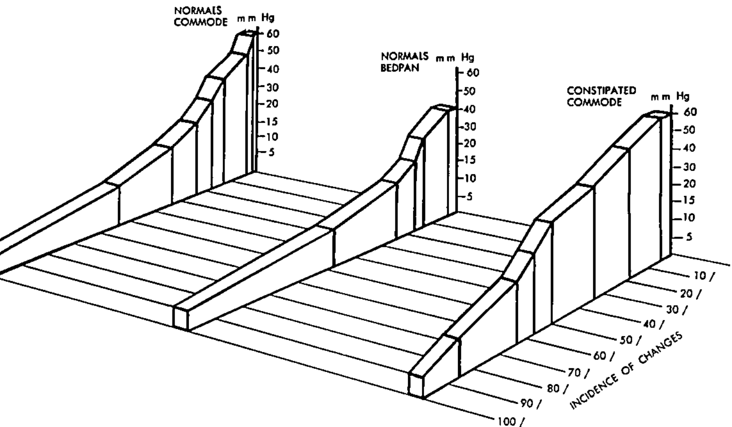
The duration of the individual pressure rises of the normal group is relatively short The constipated subjects straining for longer periods have a greater proportion of pressure increases lasting for longer intervals For all groups the increased venous pressure of both the arm and the leg drops sharply with release of the strain

The response of the venous pressure to controlled straining effort (figs 9 and 10) is more rapid in the leg than in the arm but the total net increase in pressure is similar for both The greatest changes take place within the first 13 seconds in the arm and within the first 9 seconds in the leg During any given



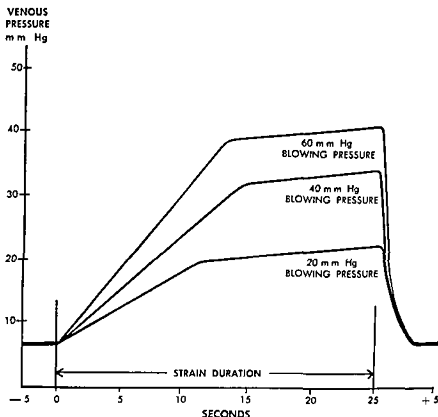
THE CUMULATIVE DISTRIBUTION OF THE ANTECUBITAL VENOUS PRESSURE INCREASES DURING BOWEL FUNCTION

FIGURE 7



THE CUMULATIVE DISTRIBUTION OF THE SAPHENOUS VENOUS PRESSURE INCREASES DURING BOWEL FUNCTION

FIGURE 8



THE EFFECT OF CONTROLLED STRAINING ON THE ANTECUBITAL VENOUS PRESSURE

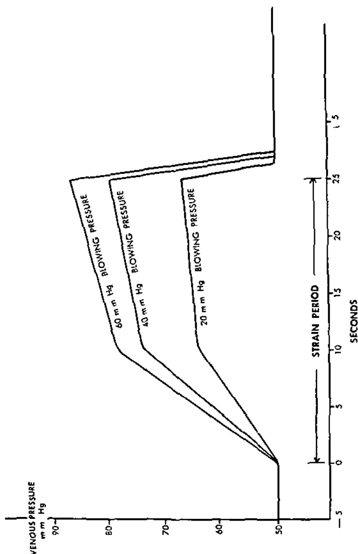
FIGURE 9

strain as the venous pressure increases the unit rate of change decreases The greater straining efforts cause greater venous pressure increases

The Effects of Straining on Segmental and Digital Peripheral Blood Flow

Only some of the straining efforts modify the segmental blood flow in contrast to the almost universal effect of individual strains on the venous pressure

The peripheral blood flow drops precipitously in both the arm

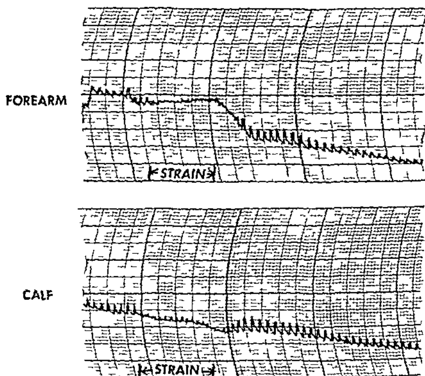


THE EFFECT OF CONTROLLED STRAINS ON THE SAPHENOUS VENOUS PRESSURE

FIGURE 10

and leg almost immediately with the institution of certain strains (fig 11) The magnitude of decrease in blood flow during a single episode is approximately the same for both the forearm and calf (The calf more often has the greater decrease than the contralateral forearm)

The magnitude of the reduction of the volume flow appears to be related to the intensity of straining. The constipated group which has the greater incidence of higher straining efforts also has the larger incidence of episodes of diminished blood flow



SEGMENTAL PLETHYSMOGRAPHS DURING BOWEL FUNCTION

FIGURE 11

greater than 70 per cent of the prestrain level. The normal group (with less intense straining efforts) has a lesser number of such decreased blood flow episodes at the commode but the use of the bedpan increases the frequency of reduced blood flow episodes among them to approximate that of the constipated series.

A vasoconstriction follows the release of the strain, the degree of which is proportional to the straining blood flow response. The greater the decrease in blood flow during the strain period, the

greater the magnitude of the post strain reduction in blood flow The duration of the post strain vasoconstriction is apparently not related to the magnitude of either this post strain decrease or the preceding reduction in flow during the strain

Those exertions capable of initiating the Valsalva maneuver are principally responsible for the modification of segmental blood flow (fig 12) Strains of lesser magnitude (10 to 20 mm

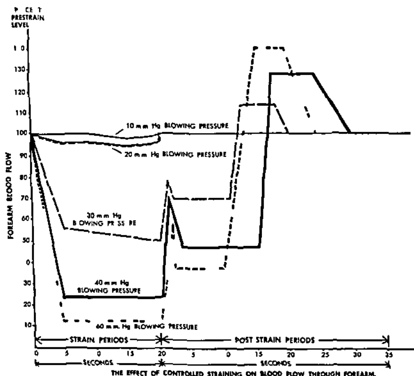


FIGURE 12

Hg) cause only minimal insignificant decreases in blood flow However with those straining efforts exceeding 30 mm Hg there is a prompt sharp drop in volume flow The greater the straining effort the greater the response in diminished flow With the termination of the effort a rapid return toward the

pre strain level takes place The post strain vasoconstriction is followed by a marked vasodilation after which the blood flow finally returns to the pre strain level

While the magnitude of response to the straining effort is approximately the same for both upper and lower limbs the blood flow through the calf is generally about 5 to 11 per cent less than through the forearm The magnitude of the post strain vasoconstriction is also approximately the same for both upper and lower limbs and again the greater response occurs in the legs

With the beginning of controlled strains a sharp drop occurs in both the blood flow and pulsation volume in the digital circulation the levels of which are sustained throughout the straining period The greater reductions occur following strains of higher magnitude The maximal drop in digital flow is achieved within one to four seconds and within the bounds of minor fluctuations remains constant for the strain period regardless of the duration of the exertion Lowering of the digital flow is greater in the toes than in the fingers

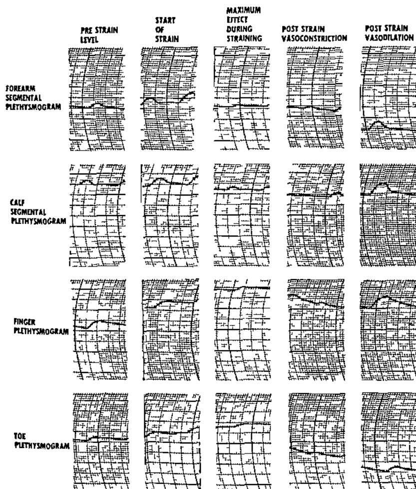
The pulsation amplitude is similarly affected by the strain effort (fig 13) A decrease in pulsation volume takes place for the finger and for the toe with the greater decreases occurring after the higher exertions A reduction in pulsation amplitude is larger for the toe than for the finger

An abrupt rise in both digital flow and pulsation amplitude occurs immediately after the release of the strain but within one to three seconds these decrease with the development of a post strain vasoconstriction The variability of response is comparable with strains of different magnitude The constancy of change during the post strain period is reflected in both the digital blood flow and digital pulsation amplitude ratios While there is some variability in the ratios during the strain period there is virtually none during the post strain period for the different levels of exertion

Following the post strain reduction in flow a rise in both blood flow and pulsation amplitude occurs There is a similar order of constancy for the digital blood flow ratio (finger to toe) and the digital pulsation amplitude ratios (finger to toe) during

FIGURE 13

CHANGES IN THE PULSATION AMPLITUDE OF THE SEGMENTAL AND DIGITAL PLETHYSMOGRAM DURING CONTROLLED STRAINING



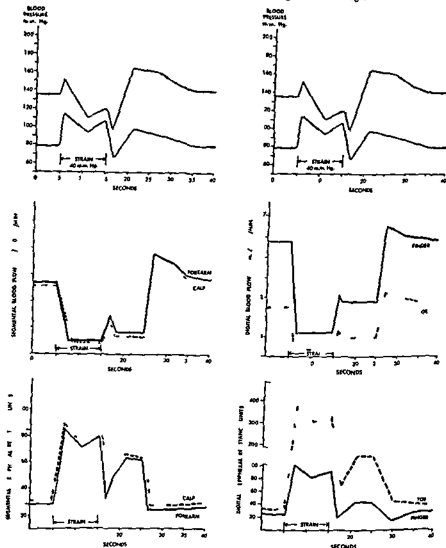
the period of vasodilation compared to that observed for these indices during the post strain vasoconstriction

The Effect of Straining on the Peripheral Vascular Resistance

The peripheral resistance is a function of the mean blood pressure and the segmental (or digital) blood flow The dynamic

FIGURE 14

The Effect of Cont olled St aini g on the Periphe al Vascular Resistance in both the S gment and Digit



effects of straining on the peripheral resistance are related to the progressive changes of arterial pressure and blood flow (fig 14)

With the start of the strain (Valsalva phase I) there is an

abrupt rise in blood pressure and thus an equally sharp rise in peripheral resistance as the blood flow is dramatically reduced With the sustained reduction in volume flow the peripheral resistance is reduced somewhat as the pulse pressure narrows and the arterial pressure falls A second increase in peripheral resistance occurs during phase II and although the volume flow remains at virtually the same low level the blood pressure rises as the pulse pressure continues to narrow With the release of the strain (phase III) both the arterial pressure and the peripheral resistance fall while the minute blood flow increases

The abrupt fall in blood pressure with the release of the strain initiates a post strain reflex vasoconstriction resulting in an increased vascular resistance which reduces the peripheral blood flow The phase IV arterial blood pressure overshoot is soon followed by an increase in volume flow which reflects the reduction in peripheral resistance during the period of post strain vasodilatation The return of the blood pressure to the pre strain level is reflected in both the peripheral resistance and volume flow which assume their basal levels

The dynamics of circulation through the forearm and calf are paralleled in the finger and toe However while the magnitude of the vascular changes in the arm and leg are approximately the same they are strikingly different in the digits with the responses in the toe being much more pronounced than in the finger Thus at peak levels the peripheral resistance in the toe is four times that in the finger

DISCUSSION

The cardiovascular system is subjected to stress during the Valsalva maneuver It is assumed that the rise in systemic arterial blood pressure at the initiation of the strain (phase I) is associated with the increased output of the left ventricle caused by blood being forced into it from the pulmonary circuit The sustained elevation of the intrathoracic pressure then acts to prevent the venous return to the heart from the pulmonary circulation and the extremities and consequently the arterial blood pressure falls This is reflected in marked through gradual elevations of the venous pressure[13,14] which are believed to

reflect in turn the pressures developed within the thorax The delay in circulation time occurring with strains satisfying the Valsalva criteria confirms the observations of interference with the venous return to the heart induced by elevated intrathoracic pressure

The acceleration of the heart rate during phase II and the slowing during phase IV are presumed[10, 13] to be of reflex origin as compensation for the changes in blood pressure and cardiac output The response of the heart rate to minimal pressure stimuli (those not satisfying the criteria of the Valsalva maneuver) is factual support of the concept that other cardio regulatory reflexes originating in the receptors of the carotid sinus and the aortic arch which respond to weaker stimuli may play an important role in governing the heart rate

The decreased pulmonary return to the heart also affects coronary circulation by reducing the aortic diastolic pressure and the left ventricular output The clinical significance of these alterations of the cardiovascular dynamics becomes especially important when the individual hazards are considered The decrease in coronary circulation during the Valsalva maneuver *and its consequent effects poses a specific threat to the patient* predisposed to coronary disease

The peripheral circulation is subjected to stresses during bowel function which become exaggerated in constipated individuals The response of the venous pressure to straining is often slower in the upper extremities than in the lower limbs This difference in rate of response may be attributed to the non dependent status of the veins of the arm in contrast to those of the leg The marked elevations of the arterial blood pressure may constitute a serious problem to those with inelastic atherosed vessels unable to accommodate for these sudden extremes in blood pressure variation

The change in venous pressure appears to be independent of the arterial blood pressure fluctuations which occur during the Valsalva maneuver While the arterial blood pressure alternately rises and falls during the various phases of the Valsalva maneuver the venous pressure maintains a persistent high level throughout the entire strain period returning to the resting state levels within seconds after termination of the strain

This apparently uniform response of the venous circulation to sudden elevations of intrathoracic pressure becomes of special significance when both the strain and the post strain effects on the segmental and digital blood flow are considered Since the presence of normally functioning valves in dependent veins prevents retrograde flow of venous blood into the lower extremities the rate of venous pressure rise depends primarily upon the rate at which blood passes through the capillaries and arteriovenous shunts The pressure of blood in the distended veins inhibits the flow of blood from the arterial and capillary circulation and this is responsible for a lower rate of venous pressure elevation as the veins become more distended

Another determining factor limiting the rise of venous pressure is the resistance to venous flow imposed by the elevated intrathoracic pressure It has been noted[14] that the increase in venous pressure reflects the rise in intrathoracic pressure during the straining effort and rarely exceeds the pressures within the trunk [16] Thus a breakthrough of the venous flow is possible when the pressure within the veins becomes sufficiently high The venous escape would then stabilize at the pressure levels in the trunk

The decreased segmental and digital blood flow during and immediately after the straining period as well as the post strain vasodilatation are reflexly controlled Thus immediately after the first few ventricular beats exhaust the pulmonary reserve the arterial pressure begins to fall and reflex vasoconstriction then maintains the peripheral circulation

This ultimately results in the return of arterial blood pressure (during phase II of the Valsalva maneuver) With the subsequent profound drop in blood pressure after release of the strain (phase III) comparable vaso receptors respond to produce vasoconstriction Similarly the systolic overshoot (phase IV) following the sudden release of the dammed up pulmonary venous blood which then returns to the left heart results in the post strain vasodilatation Thus we have a vasoreflex ebb and flow in response to straining as in defecation

The changes in segmental and digital arterial blood flow are reflections of the peripheral resistance and largely determined

by vasomotor reflexes The striking difference in the degree of peripheral resistance between the toe and the finger in response to straining may offer one explanation for the greater frequency of pathologic involvement in the toe as compared with the finger

The successive alterations of the peripheral circulatory dynamics during and after the straining accompanying bowel function may explain the occasional dislodgement of fragmentation of a blood thrombus Even minor changes in the velocity of the flowing blood stream tend to produce disturbances (or eddies) While a *constriction of the vessels*[17] *is equally capable of creat*ing sufficient turbulence to dislodge a thrombus the extreme fluctuation in caliber of the peripheral vessel walls during the vasoconstriction and vasodilatation phases is also capable of contributing to the freeing of loosely attached clots

The effect of venous distention during Valsalva straining with conversion of a propagated clot into an embolus has been dramatically described by Dodd and Crockett [18] These investigators note that it is very easy to imagine that this sort of reflux distention and the sudden relief of distention would produce just enough force to loosen a fragile slightly attached propagated clot

The hazards arising from straining during defecation may be eliminated to a major degree by reducing the magnitude and duration of the straining efforts This is the best practical approach for avoiding the onset of noxious circulatory changes *Desirable reductions in both the magnitude and duration of exer*tions of stool straining may be simply accomplished with the use of a neuroperistaltic constipation corrective After therapy with Senokot® both the magnitude and duration of strain of the chronically constipated patients were favorably modified and these were reduced to levels below that of the normal group

If tragic episodes are to be avoided the immediate correction of constipation becomes of special importance to patients with cardiovascular disease and to patients conditions predisposing them to possible embolization

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PHARMACOLOGIC PRINCIPLES IN THE TREATMENT OF CONSTIPATION AND DIARRHEA

F W Schueler Ph D *

INTRODUCTION

It has probably been the impression of others as in the case of the present speaker that it is usually easier to discourse in general upon a general subject or speak in a specific way about a specific subject than to speak either in a general way about a specific subject or in a specific way about a general one The fore going had always seemed to the writer to exhaust the possible tangle of approaches when facing a new subject until he was invited to speak upon the present topic Thus it is not yet clear to him whether his subject matter is either of a general or specific character or indeed whether the approach he has taken in dealing with it is either general or specific or both and if the latter in what proportions Moreover the subject matter itself which at a given time often seemed quite solid and well formed something one could bear down upon with a sense of purpose would frequently quickly and unexpectedly become fluid and flow hither and *yon in quite* an uncontrolled way into the *various* by ways of therapeutics in a most ubiquitous and alarming fashion As an aside it has gradually dawned upon the present

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speaker while closeted in effort toward the production of his contribution that the ubiquitous nature of *his* topic is but a gentle indication of the illusive nature of gastroenterology as such in its specific parts and in general

The foregoing represents obviously a confession of profound ignorance upon the part of the speaker but it is so often in the wake of realizations of ignorance that one gains enormous new respect and admiration for colleagues operating in other and hithertofore but weakly appreciated fields of endeavor Thus the speaker feels most definitely a newly born strong sense of admiration and respect for those who grapple daily in the field of gastroenterology The formulation of even the most arbitrary *confines of this field to say nothing of ordering and integrating* it seems a most formidable task!

THE RELATION OF PHARMACOLOGY IN THE THERAPEUTIC SITUATION

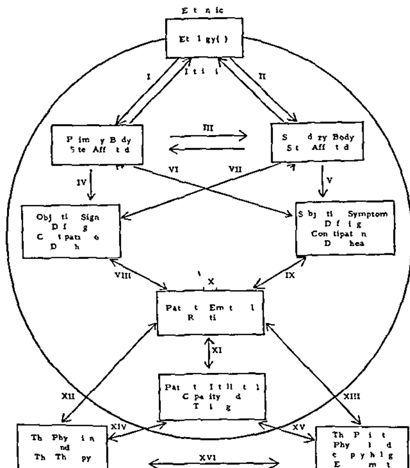
*Figure 1 represents diagrammatically the pattern or relation*ships involved in the dis eases termed constipation and/or diarrhea as they may be viewed within and about the patient "as a whole

The use of the term dis eases here for constipation and/or diarrhea emphasizes the patient s orientation rather than that of the physician Thus different patients come to the physician complaining of constipation and or diarrhea for very different objective reasons—changes in the frequency or consistency of stools presence of pain during defecation increased effort at the stool inability to retain fecal material etc Indeed no change in objective bowel habits or character of fecal discharge may be apparent but the development of headaches or other subjective experiences which have become associated in the mind of the patient with the act of bowel movements may cause him to seek the advice of a physician In any case it is the state of the patient s dis ease that becomes labelled constipation and/or diarrhea Clearly a large part of the physician s task may consist in reorienting the patient toward the semantics of the situation

Indeed such reorientation alone may be sufficient to relieve the patient

Certain aspects of Figure 1 represent matters of a subjective

Fig 1 THE PATIENT AS A WHOLE



and others of an objective nature that are either already understood by the patient or if not understood are at least representative of matters of concern to him As he assesses them toward a

synthesis of the pattern of disease he will no doubt find it necessary to base his total therapy not only upon various drugs possible surgical procedures etc but also upon making clear given aspects represented in the diagram not yet recognized or understood (or worse misunderstood) by the patient if an optimum therapeutic approach is to be attained

The Roman numerals I XVI *represent diagrammatically some* of the *dynamic phases* of interrelationship to be dealt with in the therapeutic situation Thus in the present scheme it is assumed that the actual entities (in rectangles) making up the psycho somatic entity that is the patient as a whole are to be dealt with by augmenting mitigating or even eliminating one or more of the given phases of interrelationship This *may* be *achieved by drugs toward an improved state of homeokinesis* an essential criterion of success being the relief of the person s sense of dis ease

Such a diagram is useful in the sense that it emphasizes the complexity of feedback relationships involved It reminds one that amelioration of any given phase of the patient s illness may still leave operative or even intensify some other relationship so *that the patient may on occasion feel worse off following therapy* than before therapy was begun

Now one cannot speak of sixteen complex phases of therapeutic relationships in one breath Some manner of itemization in approach must be adopted In the present description only pharmacologic principles have been considered and moreover these in but a general way as the number and variety of drug *agents of possible value in one or more of the phases of such* therapy are very large In order however that the discussion not be completely abstract in its development *two specific situations* involving the signs and symptoms of diarrhea and constipation have been chosen The first which shall represent pharmacologic principles in the treatment of diarrhea concerns therapy in ulcerative colitis The second which shall represent pharmacologic *principles in the treatment of constipation* concerns therapy in colon consciousness accompanied by constipation

THE TREATMENT OF DIARRHEA IN ULCERATIVE COLITIS

There is little that drug therapy can offer here toward attacking any discrete material etiology of this disease This is because the disease appears to have no discrete material etiology but rather appears to be rooted in a vast complex an intrinsic and extrinsic matrix of dynamic relationships that ramify as ubiquitously throughout the patient s interpersonal life as do the primary and secondary organic manifestations of the disease itself within his body Thus by this single example ulcerative colitis one sees how ultimately inadequate is any single such diagram as presented by Figure 1 that would embrace all concepts of etiology" in a discrete sense Indeed the term etiology may stand not for a thing in itself but rather for a complex manner of relationships involved within an individual and between the individual and his environment (i e I may be identical with XI XIII)

From another standpoint the present example is instructive for it is a basic principle of pharmacology that drugs can only modify the balance of existing functions they cannot create new functions This leads one to ask at what points in the diagram drugs through their ability to augment or diminish a given function may lead toward a more satisfactory state of being in such a complex disease as ulcerative colitis At least a few possibilities suggest themselves

Whatever the precise etiology of the disease the clinical picture at the time the patient seeks help often reveals an extensive area of diseased rectum and colon with breakdown of the mucosa severe diarrhea and hemorrhage which are implied in the diagram through the processes labelled IV Accompanying the objective signs defining the disorder are those of more immediate concern to the patient arising through II III and VI which define his subjective sense of dis ease Aggravating or mitigating as the case may be are the influences through XV XIII VIII XI and IX all of which control the patient s reactions objectively and subjectively Thus to one patient the sight of blood in his stool (through VII) may be less disturbing than his mother frantically calling up a physician In any case unconscious (e g autonomic) feedback (X) to both primary and

secondary sites of involvement may not only potentiate the immediate primary and secondary signs and symptoms but worse set up a pattern of a cyclic nature that as it is repeated upon subsequent acute bouts of the disorder becomes as much or even more of a problem for the physician than anything else with which he has to deal in such cases

Opiates may aid in controlling the acute fulminating phase of the disease by providing relief from the severe diarrhea Sedatives provided pain is already well controlled may be used to quiet the patient and especially his family The value of spasmolytic drugs in such situations is a matter of much divided opinion Certainly complications such as bacterial infection are matters to be controlled as soon as possible by chemotherapy but such agents do not appear to aid in the resolution of the basic disease process of ulcerative colitis Likewise in the case of very severe toxic and progressive colitis the steroid hormones may be lifesaving but should be used only in emergency Complications of continued steroid therapy involve liver abscess multiple ulceration of the ileum and giant ulcer of the cecum with hemorrhage More seriously mental depression encountered in their use sometimes has led to suicide

Overall it is evident that pharmacotherapy must operate along the already present complex of functions toward relief in the therapeutic situation At the present time in the absence of any distinct point of attack for an appropriately designed drug agent therapy must be directed at controlling the gross objective signs of this severe form of diarrhea and at setting the patient and his socio psychologic environment at ease

The corollaries here for psychotherapy on the part of the patient proper diet and supportive therapy as well as aids toward the improvement of the socio psychologic environment are many but quite beyond the scope of the present brief discussion Moreover the fact that chronic ulcerative colitis tends to become a disease of the whole person which is to say that in time it comes to involve many other tissues of his body which will as they arise involve other special forms of therapy (drug and otherwise) can only be stated here

THE TREATMENT OF CONSTIPATION IN THE COLON CONSCIOUS INDIVIDUAL

Here is an area or should one say a volume which has resisted many a mighty effort to be dislodged from its firm binding in the public repository of anxiety and misinformation Thus to just what extent colon consciousness should be considered a dis ease possessed by a patient or a patient possessed by a disease is still a moot point In short the problem of therapy involves at least in part the question to just what degree disease exists and to what degree merely dis ease

It has been said* that the colon conscious individual is so often the person who approaches the physician as though the latter s " mind s eye is ever steadily fixed upon the standard stool encased with the meter bar in Paris Whatever may be the case the colon conscious constipate comes armed with an alarm ing quantity of misinformation concerning autointoxication " the value of elaborate bowel washes and various purgatives as well as a complex ritual and liturgy to match He or she as the case may be if an adult with family has already probably fully indoc trinated the other members especially the children of the house hold and the need to justify all of the to do that this elemental operation entails makes the patient very resistant to any counsel that would seek relief through a more moderate attitude That the difficulties involved are located to a greater extent in the brain than in the bowel is usually a most unwelcome concept Thus from the standpoint of pharmacology the prescription of more drugs and procedures is usually welcomed with enthusiasm while what may actually be in order is quite the opposite

The pharmacologic principle to be adopted becomes in fact a paradox for it would better be termed an *anti pharmacologic* principle of attack Perhaps one of the first approaches (if drug therapy is to be continued at all) might be the prescription of a *new and excellent* (but actually less drastic cathartic) with emphasis that this new agent is so effective that the patient can shortly taper off on its use provided certain simple dietary meas ures and exercises be adopted The latter may serve eventually

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* H BECKMAN *Treatment in General Practice* Philadelphia Saunders 1948

as a harmless substitute for the routine of massive water drinking roughage eating daily enemas and/or purges that previously occupied the patient Again from the pharmacologic standpoint there exists no evidence that turpentine enemas calomel croton oil or other time mishonored drastics and blasters have any place in modern medicine Surely the whole concept is to wean the patient away from methods, materials and habits that are harmful He may thereby in time be taught to have a bit more confidence in his own colonic smooth musculature and pride in this may take the place of a purge even in his psyche

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As the reader may have gathered the point of view of this writer is summarized by that principle of pharmacotherapeutics in the treatment of diarrhea and/or constipation which states that drugs are more likely to be misused than not used

PSYCHODYNAMICS OF CONSTIPATION AND DIARRHEA

HENRY F ALBRONDA MD *

The subject Psychodynamics of Constipation and Diarrhea will be divided into three portions The first will consist of some general remarks concerning the anatomy physiology and pathology of the psyche The second will consist of some general remarks concerning symptom formation and more specific remarks concerning the two symptoms constipation and diarrhea The third will deal with some aspects of diagnosis and treatment of the psyche

As soon as I a psychiatrist used such scientific terms as anatomy physiology and pathology which command such medical respect some of you listening might immediately make the comment This is probably another one of those psychiatrists with his head above the clouds! How can he use such scientific words as anatomy physiology and pathology of the psyche? One cannot see the psyche on an anatomy table you cannot cut it into little pieces on a microtome stain it and look at it under a microscope! If you can t see smell taste hear or feel it how can he talk about the anatomy and physiology of the psyche! And pathology! how can he talk about pathology when he has not convinced us of the anatomy and physiology?

The foregoing remarks were only made to point up the need for a commonly shared vocabulary between people so that mutual

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as a harmless substitute for the routine of massive water drinking roughage eating daily enemas and/or purges that previously occupied the patient Again from the pharmacologic standpoint there exists no evidence that turpentine enemas calomel croton oil or other time mishonored drastics and blasters have any place in modern medicine Surely the whole concept is to wean the patient away from methods materials and habits that are harmful He may thereby in time be taught to have a bit more confidence in his own colonic smooth musculature and pride in this may take the place of a purge even in his psyche

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individual thresholds to various stimuli and when these thresholds are reached it responds to them These stimuli are perceived via the infant s perceptive apparatus Such stimuli as temperature sound light pressure and others seem to be perceived and reacted to by the infant Some investigators have said that the baby also responds to the way people feel Its behavior and feelings seem to be determined by *both* forces and seem to be shaped by them

On closer inspection the following seems to be true for the individual throughout his life The individual seems to be urged or pushed or driven by forces within and from without Over the centuries these forces have been called by various names and phrases like drives urges instincts needs soul devil spirits id cosmic forces environmental pressures planetary influence etc are familiar to us in this respect

It also seems to be true that whenever these forces exert their influence on the individual he seems to feel uneasy or perhaps *dis easy* and attempts to do something about it He learns that once the force is gratified he feels better or less uneasy At first the infant is relatively powerless to do anything about such states of uneasiness or perhaps tension himself He has to depend on his environment for relief As he develops he gradually learns ways of taking care of his own needs and/or obtaining gratification of his needs from his environment

How does he learn to do this? Most of us would agree that he learns to do this in two ways By himself and by his environment Roughly speaking the young organism because of its stage of psychic and somatic development learns in the main from its environment If the infant is uncomfortable for any reason it attempts to relieve the discomfort and automatically does so by utilizing its organ systems for doing so by crying moving sleeping eating, breathing and eliminating to mention only a few Over a period of time by experience it gradually learns to take care of its own needs and becomes less dependent and more mature

To review briefly The individual is subject to forces from within and without The forces from within and without period

understanding might proceed more easily According to the psychiatric dictionary by Hinsie and Shatzky[1] the psyche is regarded in its own way as an organ of the individual The human organism is made up of a large number of organs or organ systems, such as the cardiovascular, neuromuscular hepatic nephritic cerebral endocrinal etc There is the organ called the psyche which like other organs possesses its own form and function its embryology, gross and microscopic anatomy physiology and pathology

A word is also necessary to describe the science of mental forces in action and this word is psychodynamics

There are many theories concerning the embryology anatomy physiology and pathology of the psyche or mind and the psyche s relationship with the body or soma Reducing these theories to the simplest commonly accepted ideas today is somewhat as follows

The human organism regardless of age sex or color is subject to forces from within and from without itself and the interaction of these forces result in determining at any given moment in time what an individual thinks feels and does It is vitally important to bear in mind that the human organism is made up of many organ systems which are intimately interrelated As mentioned before the psyche or mind is only one of many organ systems that make up the human organism

At birth the human organism seems to function for the most part like it does not have a psyche but on closer examination this may not be true If one spends some time around infants in the delivery room in a hospital nursery or with new mothers one often hears remarks to the contrary Such remarks as that baby is sweet that baby has a personality of its own that infant is restless are not uncommon Some religious teachers tell us that a baby has a soul and the dictionary tells us that one of the synonyms for psyche is soul

In any event the newborn infant also seems to be subject to forces from within itself and from without itself It moves cries sleeps eats breathes eliminates and responds to the forces from without itself There seems to be evidence that it has certain

influence each other and since we know today that the soma effects the psyche and vice versa we can now turn to some of the *psycho somatic* ways of discharging tension which will take us after this rather wordy introduction to the psychodynamics of constipation and diarrhea

All or any combination of organs or organ systems may be used to discharge tension According to the Diagnostic and Statistical Manual Mental Disorders[2] the following organs and organ systems may be utilized for this purpose skin musculo-skeletal respiratory cardiovascular hemic and lymphatic gastro-intestinal genitourinary endocrine nervous system and organs of special sense

The system we are focusing on in this course is the gastro intestinal system Clinical experience and research work has shown that the gastrointestinal system is affected by psychological forces The gastrointestinal system by virtue of its taking in retaining and eliminating functions readily lends itself to psychological forces (Alexander)[3] Another factor that contributes to its susceptibility as an organ system for the discharge of tension is its rich supply of nerve fibers from the autonomic nervous system both sympathetic and parasympathetic Still another and perhaps the most important for our purposes this morning is the emotional experiences that occur around the physiological functions of the gastrointestinal system—namely eating digesting and eliminating (defecating) It is postulated that certain experiences condition the developing organism for either *case* or *dis ease of* gastro intestinal function How might this happen and what is some of the evidence for it?

The neonate seems to behave as though no boundary exists between itself and the environment As Margolin[3] puts it the initial developmental phase is characterized by a basic unity or continuum between it and its environment The environment operates for the infant as though it were an involuntary organ in its body It provides nutrition in the same sense that the liver furnishes glucose It regulates the ambient temperature to correct for the uncoordinated body heat production or loss The baby s hunger cry which activates his mother to nurse him acts

ically set up a state of tension within the individual for which he seeks relief Relief occurs when the state of tension is relieved by gratification of the need The more complete the gratification of the need the less the tension or dis ease The individual at tempts to gratify the need himself or through his environment usually both His success in doing this is determined by what he is equipped to do by virtue of the level of maturation of his organ systems and his environment at the time the tension occurs

Before proceeding further it is important to understand the various ways a human organism attempts to discharge tension after such tension develops as mentioned above It is important to remember again that we are talking about the entire human organism and only dividing it into its component parts organs and organ systems for purposes of understanding

How does the individual discharge tension?

It immediately becomes apparent that each individual has his own idiosyncratic way of discharging tension Just as individuals have their own unique set of fingerprints individuals have their own unique ways of dealing with tension Some generalizations may help us at this point just as it is helpful to know that all individuals have fingerprints before we start to identify one individual

It is generally held that there are two ways to handle tension psychologically and somatically I have never seen a pure culture of either one A moment of reflection will readily show that both methods of discharging tension for all practical purposes occur at the same time It might be helpful however to talk about the psychological method of handling tension since most of you are quite familiar with the somatic methods Psychological methods of dealing with tension include what is referred to in psychiatry as psychological defense mechanisms such as repres sion sublimation conversion denial phantasy reaction forma tion phobias delusions hallucinations illusions etc A less commonly known method of discharging tension is through the formation of character traits such as stubborness aggressiveness stinginess generousness kindness etc

Since all the organ systems seem to be related and seem to

descriptions of environmental experiences and which had led perhaps to the answer of constitutional causality or causal nihil ism She intensively studied a group of thirty eight cases among which were a preponderance of gastrointestinal cases The consistency in findings relative to maternal behavior and atti tudes are most suggestive that there are correlations between spe cific maternal behaviour and attitudes to the child and to specific organ function which affect the functioning of those organs in infancy and may sensitize the organs so that their mal functioning becomes one facet in the total neurotic mosaic

She found that the mothers of these infants with psychosomatic disorders had the following in common All these mothers were narcissistic and uninterested in the child except as a self enhanc ing asset They resented the exertion involved in child care *and rarely gained pleasure from the mother child relationship* In other words they all lacked mature motherliness In addition most were rejecting and physically cruel in various ways and resented the added care of the infant during physical illness Therefore each child presenting a psychosomatic disorder had experienced frustrated dependence at a stage when body needs are dependent upon the mother for satisfaction Only specific atti tudes and behaviour activities of the mothers which seemed to us in each case to create an environment which insulted the infant organism but which were particularly noxious to the spe cific functioning of certain organs will now be mentioned

In her study of ulcerative colitis cases she found that all the children were unwanted The mothers complained of disgust and dislike of stools and diaper changes and were particularly irritated with the childs diarrhea Bowel training in all cases had been early and punitive In character these mothers were dependent upon their own mothers They were unloving six of them being sexually frigid but were very ambitious for the childs achievement of training walking talking and pushed for independent but conforming behaviour

In her study of the cases of coeliac disease and megalocolon (with or without encopresis) she states they possessed the most disturbed of all the mothers studied Eight were psychotic

like an internal humoral stimulus which initiates an internal restitution

Thus if the neonate s needs are gratified as tension occurs the tension subsides

According to Linn [4] Spitz [6] and Ribble[7] have demonstrated that normal physical development depends upon the existence of a normal mother child relationship in infancy A normal mother child relationship is thought of here as a relationship between mother and child in which the parent (normal or motherly) responds to a disturbance of a child by trying to relieve the disturbance This might be contrasted with the parent (abnormal or unmotherly) who results this disturbance and attacks the annoying aggressor (the child) as postulated by John Rosen according to Gerard [8] In the absence of a normal mother child relationship wide spread physical alternations may develop and permanently injure the child or even result in its death [4]

Some investigators by studying both infants their parents or parent surrogates and their relationships have been able to relate disorder of organ or organ systems to a specific abnormality in the relationship Especially worthy of mention in this regard are the investigations of Spitz Ribble Gerard Alexander Margolin and others

For our purposes this morning only a few such studies pertaining to the gastro intestinal tract will be mentioned As mentioned by Linn[4] Spitz found that some cases of vomiting in the infant were considered etiologically the result of a maternal attitude of overt primal rejection three months colic from primary anxious over permissiveness fecal play from cyclical mood swings Gerard[8] became interested several years ago in studying and analyzing detailed behavior of mothers in the care of their children in an attempt to determine the influence upon ego development of minute variations in the mode of feeding of holding of supporting of bathing of talking or singing of smiling or frowning etc From such data Gerard hoped to find the answer to questions of choice of symptoms and personality characteristics which had evaded explanation from gross

a reflex sensitivity imposed that makes the particular organ or organ system potentially capable or likely to be used for expressing tension

Such situations or experiences as just described by Gerard seem to call upon the gastro intestinal system as a system for the expression or discharge or indicator of tension

Another way of helping us understand is the concept proposed by Franz Alexander [9] After intensive studies he reported that the gastro intestinal tract because of its three major functions of taking in retaining and eliminating was especially suitable for the expression of these three emotional tendencies particularly if their normal expression through the voluntary motor system were inhibited He noted some correlation between certain personality trends with different disturbances of the gastro intestinal tract and also a relationship to the part of the tract involved Thus the upper end of the tract is more suited for the expression of receptive or taking in conflicts and the lower end for retentive or giving trends

If the points mentioned so far have shed a little light on the psychodynamics of constipation and diarrhea perhaps emphasizing it a little differently might shed further light

Turning again to the situation in which organs and/or organ systems seem most likely to become conditioned the infant mother relationship You will recall that about all the neonate does is sleep eat breathe digest and eliminate providing no disease prevents it from doing so Periodically it becomes hungry and as it does so it makes its wants known If its wants are gratified the need is satisfied and tension subsides If its needs are not gratified tension remains within the organism and is discharged through its organ or organ systems as in motor restlessness insomnia crying colic vomiting etc If the experiences around feeding are not pleasant that is tension producing it is postulated that the gastrointestinal system becomes conditioned to certain stimuli and if reinforced by similar experiences throughout life comes to be used as an organ system for expressing tension I am fairly certain that most of us would agree

with depressive and apathetic behaviour interrupted by occasional violent outbursts The others were withdrawn complaining and irritable Severe reaction to constipation was described by them It elicited anger irritation and frequent enemas and suppositories often used preventively when the infant was not constipated None of these babies were breast fed most were fed with propped bottle rather than held and most were force fed" when disinterest in food was shown All of the babies were exposed to further severe physical suffering from beating slapping yelling In four cases the father was cruel while the mother passively permitted his cruelty to the child

In the duodenal ulcer cases she found that these babies "were exposed to irritable mothers who were particularly displeased with the extra care involved in illness and all three babies had frequent illnesses All three mothers were inconsistent threatening hugging then scolding shouting spanking and often shaking the child at feeding if he dawdled or such None of the babies were breast fed none were held during bottle feeding and all were on feeding routines with long intervals

The cases in Gerard s study and those cases reported by others according to Gerard only offer hints as to possible biographical experiences which may play roles in the sensitizing of different organs or organ systems so that the organs break down in later life to exhibit physical pathology

It should not be inferred that the particular factors just mentioned and quoted above represent the only determinants in organ symptom formation but as Gerard states merely that in the multiplicity of determinants these seem to play important parts

She postulated then that inadequate functioning and susceptibility of an organ may stem from the injury of the organ induced by the mothers care of the child during the physiological functioning of that organ Injury further comes about by a mother s rejection of both child and organ functioning and especially so when there is increased rejection during specific functioning of organs or organ systems as in eating defecating crying etc

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that such conditioning is possible If an infant becomes hungry and is promptly taken care of in a warm loving relaxed giving manner there is greater likelihood of gratification of the infant's needs especially the needs of the gastrointestinal tract than if the opposite is true It takes little imagination to see how the infant who is hungry is not paid attention to roughly handled force fed when not hungry not given palatable foods stimulated excessively at the time it is being fed by loud noise etc might have his gastrointestinal tract upset Contrast your experiences of eating digesting and eliminating in a quiet relaxed individually pleasant situation with the opposite situation I am fairly certain that in all of your experiences with patients who have difficulties with their gastrointestinal system you encourage them to eat foods that appeal to them in an atmosphere that is conducive to proper ingestion and digestion

The experiences the developing organism has during feeding digestion and elimination then condition how this system might function under a variety of stimuli

For our purposes the upper portion of the gastrointestinal system is conditioned in the main during the first year of life but it should be remembered that all the systems are probably being more or less conditioned throughout life I brought in the upper portion of the gastrointestinal system in this presentation because what happens to the upper end of the gastrointestinal tract also determines in part what happens to the lower end and vice versa for example gastrocolic reflex

The lower end of the gastrointestinal tract receives part of its greatest conditioning impact in my opinion around the time of bowel or toilet training that is toward the end of the first year of life Again I feel fairly certain that all of us would agree that if this natural development of bodily control is allowed to proceed in an easy relaxed gentle affectionate natural manner the likelihood for current or future difficulties in this portion of the gastrointestinal tract is less likely to occur

If the developing organism is hurried pushed too fast given certain unhealthy attitudes about such natural functions diffi

culties are more likely to occur and unhealthy patterns of reacting set up for the discharge of tension If the mothering person has unhealthy attitudes toward this organ system herself this has its influence upon the developing organism under her care If she is tense at the time of such experiences with the infant or child while this organ system is functioning it is postulated that tension is more likely to occur in the child In my opinion this has been corroborated by my own clinical experience the clinical experience of child psychotherapists who have worked with infants and mothers and some of the reports in the literature referred to above

Assuming then that such conditioning occurs throughout life and I think that such an assumption is justified in the light of what is known concerning human behavior how might this help us when as clinicians we are confronted with the patient who complains of constipation and/or diarrhea?

How does the symptom constipation and/or diarrhea come about with this frame of reference—that is psychodynamically Studies of patients with non organic constipation or diarrhea have helped us understand the mechanism somewhat as follows

When the individual comes up against a stressful situation he attempts to deal with it in the only way he knows how He comes to the stressful situation with a built in variety of mechanisms for handling tension—psychic and somatic He will automatically use the ones that he has been conditioned to use under stress If the individual has been conditioned to use his gastro intestinal system he will do so just as others might use other systems There might be hyper hypo or dysfunction of the system The clinician when faced with the problem therefore is something like a puzzle solver who in order to treat the patient scientifically needs to understand how the symptom has come about

In the complicated case this is no small task but fortunately by applying the techniques of diagnosis we were all taught an answer can usually be found by taking a careful history doing a physical examination and ordering indicated laboratory work

If you would look upon each patient as a unit made up of a

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If the developing organism is hurried pushed too fast given certain unhealthy attitudes about such natural functions diffi

practices the Golden Rule in its broadest sense—in short treat the patient as yourself would like to be treated if you were that patient Of course no one can have such an attitude always but this is the ideal toward which to strive With it the patient feels he can communicate the pertinent information the doctor needs to know

Some of you might think To take a psychiatric history would require a great deal of time and I schedule a patient every 15 or 30 minutes How can I take such a detailed history with the kind of practice I have? Though taking a psychiatric history is time consuming it is a fact which should be taken into consideration when planning your schedule If you choose not to devote your time to taking such a history it is your decision However some of your psychiatric colleagues would be willing to do it for you!

Points in the history which should alert you to the possibility that psychological factors are of prime importance in the genesis of the patient s symptoms are shifting complaints a family history of emotional instability evidence of nervous tension in childhood poor school and vocational record a long medical history which often includes numerous operations many contacts with physicians disturbances in sexual relationships and current signs of nervous tension—with or without the presence of significant organic disease If in doubt about the presence of psychopathology after the history is taken the physical examination done and laboratory tests obtained a psychiatric consultation is strongly advised

Many clinicians say they cannot get the consent of their patients to see a psychiatrist in consultation I suspect the answer to this problem lies more with the clinician than the patient since unfortunately some still feel that the psychiatrist should be called in consultation only when the patient exhibits gross signs of psychopathology If the patient is informed honestly of the reasons for the referral and the clinician is convinced of its need and deals therapeutically with the patient s concern the referral usually will be readily acceptable After such a consultation the

complex of organs and organ systems that is subject to forces from within and without and the current functioning of that organism at any given point in time is the resultant of all those forces, we might have a point at which to begin helping that patient When one understands what is causing the symptom the treatment then becomes apparent One of my teachers recently mentioned that the meaning of the word diagnose is to know thoroughly or to know through and through

I would urge you to remember that the patient in addition to all his other organ systems also has a psyche and that in order to know a patient through and through all his organ systems including the psyche and their influences on each other need to be studied

Most physicians have had adequate training and experience in learning how to scientifically study and treat the various organs and organ systems with the exception of the psyche How this exception has come about need not concern us here I would like to mention however that the technique of examining and treating the psyche can be learned and it might be helpful for you to know that many of us are attempting to teach it in undergraduate and post graduate training programs

If you happen to run into patients whose gastrointestinal system disturbance does not seem to be caused by some organic disease or seems to be maintained or influenced by psychological factors and if you are in doubt it might be helpful to the patient to be referred for a psychiatric consultation in hopes of clarifying the diagnosis

Sometimes for one reason or other psychiatric consultation is not feasible or practical Under such circumstances the clinician might wish or be compelled to examine and treat the psyche himself

Taking a history of the psyche can be learned and if practiced —preferably under expert supervision—one can become quite skillful and proficient Of paramount importance in the taking of the psychiatric history is *your* attitude toward the patient The ideal attitude is best described by the attitude of the person who

GENERAL CONSIDERATIONS OF GALLBLADDER AND BILIARY TRACT DISORDERS

J EDWARD BERK M D Sc D *

A vast amount of knowledge has been amassed regarding dis eases of the gallbladder and biliary tract Much remains to be learned however and opinion concerning certain aspects of these disorders is still not unified Moreover advances in diagnosis and treatment continue to be made For these reasons it would seem advisable from time to time to review current methods of study and existing attitudes and opinions in order to appraise them in the light of accumulated experience

CLINICAL FEATURES

Significance of Dyspeptic Symptoms So-called flatulent gaseous or qualitative dyspepsia and the aphorism fair fat forty and belches have become so firmly associated with gall bladder disease in medical thinking that patients with these symptoms are immediately suspected of having gallbladder dis ease This is evidenced by the frequency with which radiologic examination of the gallbladder is requested in patients with such symptom configurations In a study of 100 patients referred to the Radiology Department of the Einstein Medical Center for cholecystography with a tentative diagnosis of gallbladder dis ease Eskin and Tumen[1] found that only 27 had an abnormal

* As te Professor of Clin cal Medicine Wayne State University College of Med c ne Detro t

presence or absence of any psychopathology which may play a part in the patient's complaint will be clarified and the patient can be started on the road to help.

Management of the patient with constipation and/or diarrhea then is determined by the definitive diagnosis. If he needs medical, surgical, or psychiatric treatment—or any combination of these—he can be so informed and allowed to choose. To me it is not a question of either/or but rather the diagnosis and the best treatment for the patient.

A recent developing trend, and I think a very productive one, has been the development of programs that are geared to training the nonpsychiatric physician to examine and treat the psyche.

Those of you who might be interested in reading further about *the Psychosomatic Mechanisms in Constipation and Diarrhea* are referred to an article so titled by Dr. Daniel S. Jaffe (10) which was published in the *American Journal of Proctology*, volume 8, number 3, in June 1957. This article is mentioned not only for its technical detail but also for its excellent references.

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A vast amount of knowledge has been amassed regarding dis eases of the gallbladder and biliary tract Much remains to be learned however and opinion concerning certain aspects of these disorders is still not unified Moreover advances in diagnosis and treatment continue to be made For these reasons it would seem advisable from time to time to review current methods of study and existing attitudes and opinions in order to appraise them in the light of accumulated experience

CLINICAL FEATURES

Significance of Dyspeptic Symptoms So-called flatulent gaseous" or "qualitative" dyspepsia and the aphorism fair fat forty and belches have become so firmly associated with gall bladder disease in medical thinking that patients with these symptoms are immediately suspected of having gallbladder dis ease This is evidenced by the frequency with which radiologic examination of the gallbladder is requested in patients with such symptom configurations In a study of 100 patients referred to the Radiology Department of the Einstein Medical Center for cholecystography with a tentative diagnosis of gallbladder dis ease Eskin and Tumen[1] found that only 27 had an abnormal

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cholecystogram. In a similar survey conducted some 15 years later by Strygler and Berk at the Sinai Hospital of Detroit[2] only 21 of 100 such patients proved to have an abnormal cholecystogram. Of striking interest in the latter study was the fact that of the 24 patients with an abnormal cholecystogram only 2 had no symptoms other than flatulent dyspepsia. Hinkle and Moller[3] after examining the symptoms described by 1000 patients referred to the Radiology Department of the Geisinger Memorial Hospital for cholecystography, were likewise unable to find any correlation between the symptoms of qualitative dyspepsia and the cholecystographic findings. Indeed, excessive belching and gas, vague upper abdominal pain, and intolerance to cabbage, pork, ice cream and fatty foods were encountered by them somewhat more frequently in subjects with normal cholecystograms than in those with cholecystographic abnormalities. In a study approaching this problem from a different direction, Colcock and McManus[4] found that only 4.9% of 1356 patients operated on at the Lahey Clinic for gallbladder and biliary tract disease complained solely of dyspepsia prior to operation.

Sight is often lost of the fact that gaseous or flatulent dyspepsia is not specifically related to disease of the gallbladder. Even in those with demonstrated gallstones dyspeptic symptoms may not be due to the cholelithiasis but may arise instead from some other cause or coexistent disorder. Erroneous incrimination of the gallbladder as the cause of dyspeptic symptoms is probably responsible for a distressingly large proportion of the patients who experience unsuccessful results from cholecystectomy. It is highly important, therefore, to restrict cholecystectomy in patients with dyspeptic symptoms to those with unequivocal evidence to support a diagnosis of chronic disease of the gallbladder. It is also wise in these cases to conduct a thorough preoperative diagnostic survey to make sure that other disturbances are not present that could be responsible for digestive symptoms. In addition, it should be carefully pointed out prior to operation on patients with dyspeptic complaints that these symptoms may not be arising from the gallbladder and may even persist following cholecystectomy.

The Importance of Biliary Colic The outstanding symptom of disease of the gallbladder is biliary colic. This is attested to by the fact that of the patients in the group studied by Eskin and Tumen[1] who subsequently were demonstrated to have gallstones all but one had biliary colic as a symptom. Similarly 20 of 24 patients in our group with abnormal cholecystograms had pain as a symptom. The study earlier referred to by Hinkle and Moller[3] provides additional evidence supporting the importance of abdominal pain as a symptom of demonstrable organic disease of the gallbladder. These investigators found that right upper quadrant colicky pain was the only symptom showing positive correlation with the cholecystographic findings.

Because of its importance as a symptom of gallbladder and biliary tract disease, a definition and description of what is meant by the term "biliary colic" would appear to be in order. The term itself is actually a misnomer. The pain of biliary colic is essentially constant and lacks the remittency of true colic.

Classically, the onset is abrupt with the pain rising in a crescendo-like fashion to reach more or less of a plateau. Once it attains its peak the pain persists. However, it may vary somewhat in its degree of intensity and thereby simulate colic. The initial location of biliary colic most often is in the high epigastrium and not the right upper quadrant.[5] Biliary colic ordinarily is promptly relieved by the administration of an analgesic or by spontaneous correction of the situation responsible for its production. Failure of the pain to respond to the parenteral administration of an opiate, or its rapid return after a potent analgesic has been given, should arouse suspicion that the underlying gallbladder disorder is complicated or associated with some other disease process.

Dangers of Acute Cholecystitis and Complications of Chronic Cholecystitis in Elderly Persons It has come to be appreciated that gallstone disease in the elderly constitutes a real hazard to life. The death rate in older people with gallbladder disease has been shown to be significantly greater than in those of the same age without cholecystic disease.[6] Acute cholecystitis occurs more frequently in the aged[7,8,9] and gangrene and perforation may

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(fig 1) Juniper and Burson[12] in a recent re appraisal of the significance of these findings pointed out that an abnormal number of cholesterol crystals or calcium bilirubinate pigment or both may be found in non calculous disorders of the gallbladder and in individuals with hepatopancreatic disease However they concluded that if the serum bilirubin level and the bromsulfalein retention were within the normal range the occurrence of abnormal numbers of biliary crystals in the duodenal aspirate was strong evidence of cholecystic disease They also ascribed significance to microspheroliths to which little attention had been paid in the past It was their observation that these small crystalline structures occurred nearly always in association with calcium bilirubinate pigment They considered them therefore to have the same significance as pigment granules for clinical purposes

The identification of cholesterol crystals and calcium bilirubinate pigment requires experience and training since there are numerous other materials in the duodenal contents with which they may be confused In cases presenting crystalline material simulating cholesterol identification of cholesterol may be possible through the use of the staining technique described by Machella[13] This technique basically involves the application of concentrated sulfuric acid to the edge of the coverslip containing the washed duodenal sediment On contact with a cholesterol crystal the acid yields a reddish violet color resembling the end point of the reaction used in the chemical method for determining serum cholesterol

Although roentgenologic examination of the gallbladder and biliary tract has largely supplanted duodenal biliary drainage the latter should not be entirely discarded It is especially valuable diagnostically in patients whose gallbladders fail to visualize by x ray and in those who have undergone cholecystectomy Block and his associates at Henry Ford Hospital[14] have provided evidence of the continued usefulness of this procedure in cholecystectomized persons suspected of choledocholithiasis Of 37 such patients who were operated on by them and proved to have choledocholithiasis 16 (43) had positive preoperative diagnostic findings of gallstones by biliary drainage

While diagnostic biliary drainage is valuable in those with

develop in such persons with a minimum of physical signs The recovery rate of common duct stone is greater in older than in younger persons [9,10] The possibility of finding cancer of the gallbladder is also significantly greater in those with calculous cholecystitis over 65 years of age than in those of younger age [10]

These findings with respect to the increased incidence of acute cholecystitis and the high rate of serious complications of chronic cholecystitis in elderly persons bear importantly on the decision to be made with respect to the treatment of gallbladder disease in these people They also bear importantly on the attitude to be adopted toward so called silent gallstones in younger persons about which more will be said later

LABORATORY AIDS IN DIAGNOSIS

Duodenal Biliary Drainage Most clinicians with long experience in the use of duodenal biliary drainage for diagnostic purposes will attest to the continued validity of the data first advanced in 1931 by Bockus Shay Willard and Pessell [11] These



Fig 1 Calcium bilirubinate pigment and cholesterol crystals in duodenal sediment obtained by biliary drainage

investigators clearly established that the finding of cholesterol crystals and/or calcium bilirubinate pigment in the duodenal aspirate provided strong evidence of the existence of gallstones

arising from this cause have been sharply reduced with the introduction of improved contrast media and the use of supplementary methods of study in such cases



Figure 2



Figure 3

Fig 2 Plain film of abdomen showing opaque calculi filling gallbladder cystic and common bile ducts

Fig 3 Oral cholecystogram showing layer of radiolucent calculi in opacified gallbladder

It is wise to avoid drawing final conclusions with respect to the function of the gallbladder when visualization is not obtained following the routine dose of even the newer contrast media Mellinger and Pearson [6] for example found that 35 8% of 67 patients whose gallbladders failed to visualize on the first study and who had at least one subsequent examination showed a well visualized gallbladder on one of the repeat studies In our experience at Sinai Hospital of Detroit [1] approximately one third (32 8%) of a group of 98 patients whose gallbladders failed to visualize following the conventional dose of iopanoic acid (Telepaque®) showed a well visualized gallbladder on repetition of

jaundice in whom roentgenologic study is precluded it must be borne in mind that the finding of calcium bilirubinate pigment alone in the presence of jaundice does not carry with it the same significance as it would if jaundice did not exist This stems from the fact that bilirubinate pigment tends to precipitate from stagnant bile in the presence of obstruction

Serum Amylase Determination of this enzyme is especially warranted in patients with acute cholecystitis because of the possibility of associated acute pancreatitis [15] Routine determination of serum amylase in such individuals may well disclose some degree of elevation in a surprising number in whom pancreatic involvement might not otherwise be suspected

ROENTGENOLOGIC AIDS IN DIAGNOSIS

Plain Film of Abdomen Considerable information of diagnostic importance may be obtained from a plain film of the abdomen in patients suspected of biliary tract disease From 8 to 30% of gallstones are sufficiently opaque to be visible on a plain film of the abdomen[16] (fig 2) Milk of calcium bile calcification of the gallbladder and emphysematous cholecystitis with gas in the lumen and wall of the gallbladder[17] are other findings that may be disclosed Still another finding of diagnostic value is the presence of stellate radiolucent fissures in the gallbladder area [16] These represent gas filled fissures within gallstones which themselves are not opaque

Oral Cholecystography Probably the single most important objective method for the diagnosis of disease of the gallbladder is oral cholecystography With present day techniques the over all accuracy of this examination is in the neighborhood of 97 to 98% [18] The greatest degree of accuracy obtains when the study specifically demonstrates the presence of stones polyps or other tumors [18,19] Diagnostic accuracy is lessened somewhat when the gallbladder is non functioning and is also lessened when the gall bladder appears to be normal [18,20] The inaccuracy of the examination is maximal however when the diagnosis is based only on what appears to be poor functioning of the gallbladder Errors

TABLE 2

FREQUENCY OF VISUALIZATION OF BILE DUCTS
DURING ORAL (TELEPAQUE®) CHOLECYSTOGRAPHY

Cholecystogogue	*No Cases*	*No With Ducts Vis*	%
Cholex[1]	2537	1452	57 2
Gall Prep[2]	67	53	79 1
Gall Prep S[3]	21	15	71 4
Saff[4]	46	33	71 7
Cholecystokinin[5]	49	40	81 6

[1] Aqueous emulsion of egg yolk soya lecithin glycerin and peanut oil (Bell Craig Inc)

[2] Aqueous emulsion of refined corn oil (Gray Pharmaceutical Co)

[3] Aqueous solution of d Sorbitol (Gray Pharmaceutical Co)

[4] Aqueous emulsion of safflower oil (Abbott Laboratories)

[5] Pancreozymincholecystokinin (SQ9662)—For intravenous use—(Supplied for investigational study by E R Squibb & Sons)



Fig 4 Appearance of cystic and common bile ducts 8 minutes after intravenous administration of cholecystokinin (3 0 mg) in a patient whose gallbladder had been opacified with Telepaque® (Berk J E and Feigelson H H *Bull Sinai Hosp of Detroit* Vol 5 1957)

the examination using a double dose of the same medium (Table 1) It must be mentioned in this regard that double dose"

TABLF 1
VALUE OF DOUBLF DOSE STUDY IN ORAL (TELEPAQUE®) CHOLECYSTOGRAPHY

No Cases Gallbladder Non Vis With Single Dose	No Cases Gallbladder Vis After Double Dose
98	32 (32 8%)

(Double Dose = 2 x single dose up to maximum of 6 gm (12 tabs))

appears to be a loosely used term with variable meanings In our hands a double dose study consists of the administration to the patient of twice the amount of contrast medium initially given The maximum amount of iopanic acid (Telepaque) which is given as the double dose however has been more or less arbitrarily restricted to a maximum of 6 grams (12 tablets) The double dose is taken the evening of the same day that oral cholecystography performed after the average dose of contrast material failed to visualize the gallbladder Roentgenograms of the gallbladder are then taken again the following morning

Spot films taken with the patient in the upright position have become standard parts of a complete and carefully performed cholecystographic study With the patient upright radiolucent stones tend to layer and form a radiolucent band within the opacified gallbladder (fig 3) It is important however to allow the patient to remain erect sufficiently long for the stones to assume a level within the contrast laden gallbladder consistent with the relative relationship of the specific gravity of the stones to that of the rest of contents of the gallbladder

Visualization of the bile ducts is today also considered an integral part of routine oral cholecystography Up until approximately 2 years ago it was our experience to visualize the cystic and common ducts after a fatty meal (Cholex®) in a little better than half (57%) of the cases in which the gallbladder was successfully opacified (Table 2) For the past two years as the result of special studies that we conducted on the influence of various

seen Visualization of the ducts in these circumstances may be taken as evidence that the gallbladder is significantly diseased or that the cystic duct is obstructed since the appearance of the contrast medium in the ducts is evidence in itself that the material had been absorbed from the gut and excreted in proper fashion by the liver

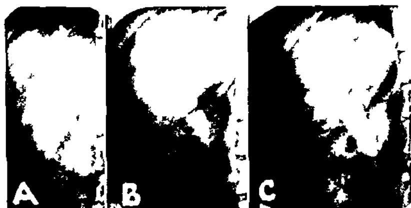


Fig 5 A Cholangiogram taken 16 hours after ingestion of initial dose of Telepaque® (6 tablets at 6 p m and 6 tablets at 11 p m) B Cholangiogram in same patient after intravenous injection of Cholografin® C Cholangiogram in same patient 30 minutes after B and 30 minutes after subcutaneous injection of 10 mg of morphine sulfate

Salzman Watkins and Rundles [8] have recently described an interesting observation which they have called the rim sign" In a few patients whose gallbladders had failed to visualize or had only faintly visualized after the conventional examination with 3 grams of orally administered iopanoic acid (Telepaque®) the ingestion on 4 successive days of 3 grams of Telepaque® daily one gram after each meal succeeded in disclosing the presence of biliary stones on films taken on the morning of the fifth day The stones were identified by having a generalized faint increase in over all density but more especially by the sharp increase in linear density which outlined the periphery of the stones This opacification of the rim of the stones occurred even though the common bile duct itself did not become visible

cholecystogogues and the optimum time for visualizing the bile ducts after their administration [22] we have significantly increased the incidence of visualization so that it is now in the neighborhood of 75% (Table 2) We found that for routine purposes a single exposure taken between 15 and 20 minutes after administration of an effective cholecystogogue is most productive

A significant advance in the study of the bile ducts after oral cholecystography has been the introduction of a cholecystokinin containing preparation suitable for intravenous administration Opacification of the bile ducts is usually evident within one minute after intravenous injection and maximal opacification is generally attained within 10 minutes (fig 4) Using a single film taken at 8 minutes following intravenous administration of this cholecystokinin preparation we were able to visualize the bile ducts in 82% of the 49 patients whom we have studied in this fashion to date (Table 2) Cineradiographic examination of the bile ducts has been carried out in some of the patients given intravenous cholecystokinin but thus far we have been unable to confirm the presence of peristalsis in the common bile duct as described by Burnett and Shields [24] It is only fair to add however that our observations have been hampered by technical limitations which we have encountered in performing this examination

New and improved contrast media continue to be developed The most recent preparation to appear is bunamiodyl (Orabilex®) Initial observations with this medium indicate that it has the advantage of producing dense opacification without obscuration of stones [5] It is also said to be associated with a lower incidence of bowel opacities as well as with a very low incidence of undesirable side effects [5]

Oral Cholangiography Oral administration of a contrast medium after the method described by Twiss and his associates [6] may succeed in opacifying the common bile duct when the gallbladder has been removed (fig 5A) We have observed as have others that in some patients with intact gallbladders which do not visualize after oral ingestion of contrast medium the common hepatic duct and/or the common bile duct may be

Intravenous Cholecystography and Cholangiography The introduction of contrast media capable of regularly opacifying the extrahepatic bile ducts following intravenous administration has been one of the most significant advances in diagnostic roentgenology of the biliary tree within recent years This method has proved in our hands to be much superior to oral cholangiography as a means of outlining the bile ducts in patients who have undergone cholecystectomy[29] (fig 5B and 5C) We have found it useful as a supplementary examination in patients with intact gallbladders whose bile ducts were not seen during oral cholecystography[30] It has also been of value in patients whose gallbladders failed to visualize by oral cholecystography even when supplemented with a double dose study The intravenous administration of iodipamide methylglucamine (Cholografin®) succeeded in opacifying the gallbladder in about half of a group of 80 such cases which we studied[30] (fig 6) What is probably even more important stones were demonstrated in approximately two-thirds of the visualized gallbladders (fig 7) In the same group of 80 cases the biliary ducts were successfully visualized in 71 (89%) and ductal stones were disclosed in 9 (12 6%) of the visualized ducts

Still another field of usefulness for intravenous cholecystography and cholangiography is in patients suspected of acute cholecystitis This examination in such cases usually discloses opacification of the bile ducts without opacification of the gallbladder or results in non visualization of either the bile ducts or the gallbladder[31,32,3] Combined cholecysto-cholangiography and pyelography may also be conducted in cases of acute cholecystitis using a special intravenously administered medium (Duografin®)[3] This preparation contains two different contrast substances one of which is selectively taken up by the liver and excreted into the bile while the other is selectively excreted via the kidneys

TREATMENT

Present Attitude Toward Acute Cholecystitis The management of acute cholecystitis has been for many years a contro-

INTRAVENOUS CHOLECYSTOGRAPHY IN PATIENTS PREVIOUSLY WITH NON-VISUALIZED GALLBLADDERS

	42 Patients	38 Patients	80 Patients TOTAL
Gallbladder not visualized after Telepaque	42 9 tablets	38 12 tablets	80
Gallbladder visualized after Intravenous Cholografin	17 12 stones shown	21 12 stones shown	38 24 stones shown
Bile Ducts visualized after Intravenous Cholografin	39 4 stones shown	32 5 stones shown	71 9 stones shown

Fig 8 Intravenous cholecystography in patients whose gallbladders had failed to visualize by oral cholecystography (Telepaque®)

instance must be tailored to fit the needs of the individual patient[343-346]

Every attempt should be made to secure immediate hospitalization of the patient in whom acute cholecystitis is suspected This permits confirmatory studies to be made and provides the optimum setting for required treatment and continual observation Those patients with evidence of peritonitis and perforation or with such signs of imminent or threatening perforation as fever rapid pulse marked leukocytosis and a distended tender gallbladder are brought to optimal condition for operation as rapidly as possible An initial conservative regimen is instituted in all other cases with close and frequent observation of the patient

If during the first 24 to 36 hours the temperature and pulse rate continue to rise the local signs of inflammation within the abdomen increase and the leukocyte count shows progressive elevation the patient is operated on without further delay Cholecystectomy with or without choledochostomy is preferred but cholecystostomy alone may be elected if this seems wiser

If after 36 to 48 hours the temperature has not significantly diminished the pulse rate remains elevated the abdominal signs are essentially unchanged the white blood cell count is still elevated and the patient generally appears unimproved operation is again no longer delayed

On the other hand if during the first 24 to 36 hours the temperature pulse rate and leukocyte count begin to decline the abdominal signs start to regress and the clinical status in general is one of improvement a conservative regimen is maintained until all signs of inflammation have subsided Diagnostic studies are then carried out to confirm the diagnosis and estimate the extent to which neighboring structures have been affected Following this cholecystectomy with or without exploration of the common duct is performed Operation is done preferably before the patient leaves the hospital but is sometimes postponed in obese persons until there has been some reduction in weight In some cases no operation is performed because of advanced age severe

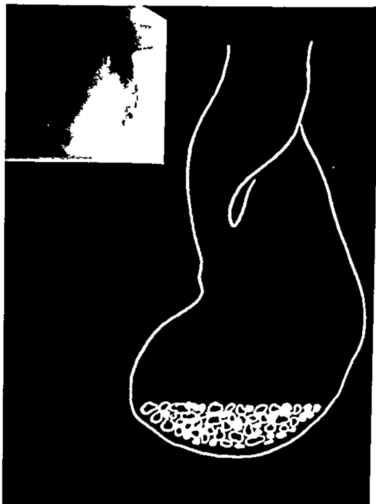


Fig 7 Appearance of gallbladder after intravenous Cholografin® (Inset) Previous double-dose study with Telepaque had resulted in non visualization Note layering of multiple radiolucent calculi

versial subject Opinion has been sharply divided in the past between those advocating immediate or early surgery and those favoring conservative management with delayed operation In recent years an intermediate viewpoint has come to the fore The basic tenet of this growing school of thought to which my associates and I subscribe is that treatment in each

bladder with a solitary stone as toward the gallbladder that contains multiple stones

Indications for Exploring the Common Bile Duct There appears to be uniform agreement on the indications for surgically exploring the common bile duct In practice however the frequency with which the bile ducts are actually surgically explored varies considerably In this connection a study by Bartlett and Waddell[42] is of particular interest Their study was based on 1000 unselected cases of cholecystectomy and choledochostomy performed at the Massachusetts General Hospital from 1943 to 1954 Previous attacks of pancreatitis jaundice alone or a reliable history of jaundice alone palpable common duct stone a dilated common duct and a dilated cystic duct proved to be accurate and urgent indexes for choledochostomy The presence of multiple small stones in the gallbladder alone however appeared on the basis of their observations to be a relatively poor indication for choledochostomy in terms of the percentage yield of stones

Complementary Use of Operative Cholangiography The perfection of this method of radiologic study has proved of great help in the detection of common duct disease at the time of cholecystectomy or secondary exploration of the common duct The demonstration by this method of examination of an entirely normal appearing bile duct with free flow of contrast material into the duodenum would appear to obviate the need for surgical exploration However it cannot be emphasized too much that operative cholangiography must be conducted with the full cooperation of the anesthetist the surgeon and the radiologist and that it must be performed with scrupulous attention to technique if it is to attain its fullest value[43] Perhaps it is only fair to add that while the degree of error is minimal when the examination is conducted under the best of circumstances this method of study is still not absolutely infallible[44]

The Problem of Overlooked Common Duct Stones The most common organic condition responsible for recurrent biliary colic jaundice or other distressing symptoms after removal of the gall

cardiovascular disease or other systemic ailments which make such surgery unwise

Attitude Toward So Called "Silent" Stone The increasing number of older persons coupled with the growing appreciation of the frequency of acute cholecystitis and the high rate of serious complications of gallbladder disease in these people have focussed attention on the matter of the proper management of so called "silent stones The great difficulty in arriving at a unified opinion on this debated subject has been the lack of data regarding the eventual outcome in patients accidentally discovered to have gallstones Truesdell[3] in 1944 reported follow up observations on 50 cases of surgically discovered quiescent gallstones which had been left undisturbed It was Truesdell's opinion that only 6% of these cases could be considered asymptomatic Comfort Gray and Wilson[38] in 1948 reported follow up observations they had made over a matter of 10 to 20 years in 112 cases of silent stone Within the period of observation 30 of the patients in this group complained of dyspepsia and 21 developed biliary colic

Much more information of this type is necessary in order to provide a sound basis for determining the likelihood of eventual development of symptoms or serious complications in those whose stones at the time of discovery appear to be asymptomatic After considering the various pros and cons of this perplexing problem Snell[39] suggested that it would appear wiser in the light of present knowledge to elect cholecystectomy as soon as stones are discovered and before complications and advanced age increase the morbidity and mortality to an unreasonable degree

Attitude Toward Solitary Stone Solitary gallstones are no longer considered a relatively innocent variety of stone Accumulated experience has made it clear that the solitary stone may produce the same signs and symptoms as those caused by multiple stones[40] Moreover the incidence of major complications in cases of solitary gallstone disease may even be greater than in cases with multiple gallstones[40, 41] It follows from these observations that the same attitude should be adopted toward the gall

duct remaining after cholecystectomy or perhaps a remnant of an incompletely removed gallbladder dilates to such a degree as to form a pouch resembling a new gallbladder In some cases these pouches are found to contain calculi which had either been



Fig 5 Intravenous cholangiogram in a patient whose gallbladder had been removed showing well visualized dilated common duct containing 2 radiolucent calculi (Berk J E and Feigelson H H *Gastroenterology* Vol 34 June 1958 Published by Williams & Wilkins Co Baltimore Md)

bladder is the presence of ductal calculi that were probably overlooked at the time of cholecystectomy.[30] The magnitude of this problem is not to be minimized. A poignant illustration is the study reported by Hicken and his associates.[46] These investigators reviewed the postoperative cholangiograms of 550 patients who had been operated on in 11 hospitals of different types in the Salt Lake City area. The operations in these cases had been performed by 26 different surgeons of varied experiences and capabilities. Of the 550 patients, 110 (20%) still harbored intraductal calculi. The incidence of residual ductal stones was 10 times as great in the 25% of patients who had been operated on by surgeons of lesser experience as it was in the 75% of patients whose operation had been performed by more experienced surgeons. *These observations point up only too well the frequency with which ductal calculi are overlooked. They also emphasize the need to employ operative cholangiography and every other available maneuver at the time of cholecystectomy to make certain that all calculi within the extrahepatic ducts are identified and removed.*

In the detection of intraductal calculi after previous cholecystectomy, intravenous cholangiography has its pre-eminent field of usefulness[30] (fig. 8). Unfortunately, however, this examination is usually of no avail in the very cases in which the information it *may provide is most desirable, namely, those with marked grades* of jaundice and/or hepatic impairment.[30] In the latter cases, duodenal biliary drainage, as discussed earlier, may prove of considerable help.

The Problem of Cystic Duct Remnants and So-Called "Re-Formed" Gallbladders. It has become increasingly apparent that disease in or about the residual stump of a cystic duct may be responsible for biliary colic and other symptoms appearing at variable intervals after removal of the gallbladder.[47] Clinical as well as experimental observations[48] have made it clear that the residual cystic duct frequently dilates following removal of the gallbladder. The term "re-formed" gallbladder has been applied to describe the situation wherein the segment of cystic

a cystic duct remnant [47] These findings indicated that cystic duct remnants are to be found in many cholecystectomized persons who are free of symptoms (fig 9) Hence the mere cholangiographic demonstration of a cystic duct remnant in a patient with postcholecystectomy distress should be interpreted as convincing evidence that therein lies the cause for the distress If the duct is markedly elongated kinked or distorted it may perhaps be suspect Visualization of calculi within the remnant however is unquestionably a significant finding

The incidence of calculi in cystic duct remnants varies depending on the source and type of material analyzed Data culled from a small series of recent and representative reports dealing with the intravenous cholangiographic findings in symptomatic and asymptomatic persons who had undergone cholecystectomy yielded an incidence of calculous cystic duct remnants ranging from 2 3% of 515 symptomatic patients whose biliary ducts were visualized to 13 6% of 44 such patients who were shown to have a cystic duct remnant [47] The surgical incidence of calculi in cystic duct remnants is even greater In a collected group of 190 patients whose gallbladders had been removed and who were found at a subsequent operation to have a cystic duct remnant roughly 30% had a stone or stones in the remnant [4] The higher incidence in the surgical series is not surprising since it would seem reasonable to assume that cystic duct remnants responsible for recurring or persisting postcholecystectomy symptoms of such severity as to require reoperation would be more apt to contain calculi

The occasional occurrence of pouches of sufficient size to constitute a re formed gallbladder is an interesting phenomenon When these structures also harbor calculi they represent perhaps the most dramatic alteration that may occur in a remnant of the cystic duct or in a partially removed gallbladder following cholecystectomy (fig 10) In a matter of some 22 months we encountered 7 patients at the Sinai Hospital of Detroit with so called reformed gallbladders containing calculi after previous cholecystectomy [4] 6 of these were identified by intravenous cholecystography while bile drainage gave evidence of abnormal

overlooked at the previous operation or which formed subsequently

In a collected series of 357 symptomatic cholecystectomized patients whose ducts were visualized by intravenous cholangio



Fig 9 Intravenous cholangiogram in a patient whose gallbladder had been removed showing dilated common bile duct and a large cystic duct remnant (Berk J E *et al* *Gastroenterology* Vol 28 Feb 1955 Published by Williams & Wilkins Co Baltimore Md)

graphy 44 (12 3%) gave evidence of cystic duct remnants[4] On the other hand in a collected series of 116 asymptomatic cholecystectomized subjects whose biliary ducts were visualized by intravenous cholangiography 18 (15 5%) were found to have

and roentgen findings in patients suspected of chronic gallbladder disease To be published

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Fig 10 Intravenous cholecysto-cholangiogram in a patient who had undergone cholecystectomy almost 5 years earlier A so-called re formed gall bladder is shown which contains several radiolucent faceted gallstones with opaque rims (Berk J E and Lee R N Am J Digest Dis Vol 3 March 1958 Published by Paul B Hoeber Inc New York N Y)

numbers of cholesterol crystals and calcium bilirubinate pigment in the seventh This experience alone we feel warrants the employment of cholecystography as an investigative study in all patients who present with postcholecystectomy symptoms It also emphasizes the need to remove carefully the entire gallbladder and as much of the cystic duct as possible when cholecystectomy is performed

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The physiological function of the gall bladder and its ducts has been very well understood for many years and does not appear to be very complex The liver normally secretes about 1000 to 1200 cc of bile each 24 hours which collects via the biliary radicles into the hepatic duct Pressure controlled by the hormone cholecystokinin elaborated by and absorbed from the duodenum governs the passage of bile through the common duct into the duodenum directly for digestive functions or through the cystic duct into the gall bladder where it is concentrated to about 1/5 of its orginal volume and stored With the ingestion of a meal the secretion and absorption of the hormone from the duodenal mucosa stimulates increased pressure in the gall bladder simultaneously with relaxation of the sphincter of Oddi and the concentrated bile stored there is passed into the duodenum to perform its digestive functions [1] We are concerned with what factors cause an interruption of this function and predispose to or cause *cholecystitis* Those most commonly believed to be of importance are infection stasis allergic reactions dietary variations and metabolic disturbances Lichtman states that The development of pathologic changes in the gall bladder depends on three main factors (1) gall stones (2) infection (3) pancreatic reflex This may be an oversimplification but it at least gives the general basis of our present knowledge Whether acute chole*cystitis* is a separate and distinct entity or the early phase of what if the gall bladder is not removed may evolve into a chronic *cholecystitis* is questionable It would appear that it is most probably an early phase of the same disease and that the same etiologic factors are to be considered

Infection may result from bacteria invading the gall bladder by ascending the bile ducts from the duodenum by direct exten*sion from* adjacent infected organs as from the pancreas by hematogenous or lymphatic circulation or by direct drainage in the bile secreted by *the liver* In so vulnerable a position it would seem unusual that invasion by bacteria does not occur more often than *is now observed* The bacteriostatic quality of bile which apparently acts as an effective barrier is the probable explanation Actual pathogenic organisms are recovered from

PATHOPHYSIOLOGY AND MANAGEMENT OF CHRONIC CHOLECYSTITIS

SAM A OVERSTREET MD *

THE presenting symptoms of gall bladder disease are perhaps as clearly defined and as well known to physicians as those of any other single disease entity Gas flatulence intolerance to certain foods and recurrent attacks of abdominal pain constitute the cardinal symptoms Abdominal distension localized tenderness palpable liver or gall bladder jaundice fever leukocytosis are variable accompaniments of acute attacks With these characteristic symptoms and signs the physicians and surgeons of a generation ago developed a remarkable acumen for diagnosis of cholecystitis and clinical experience dictated with reasonable accuracy the selection of the most effective means of treatment

The use of bile drainage by means of the duodenal tube with study of the gross microscopic and cultural characteristics of the fluid provided a more effective means of differential diagnosis Development of x ray techniques by the Graham Cole method about 1925 added immeasurably to accuracy and the more recent refinements of this method have extended the scope of our investigation We are now able to determine with a reasonably high degree of accuracy whether the organ functions and whether stones are present in the gall bladder the cystic or common ducts This proves a valuable guide as to whether treatment should be medical or surgical but it really leaves a great deal to be desired in our knowledge of the disease itself

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Disturbance of cholesterol or calcium metabolism may lead to cholesterosis with thickening and discoloration of the mucosa often characterized as the "strawberry gall bladder" This may be an acute process requiring immediate attention or may progress slowly practically symptomless until calcification of the gall bladder wall the formation of stone and obstruction of the cystic duct resuts Stasis disturbance of function or the formation of cholesterol or mixed type of stone may be the basis for chronic cholecystitis with the usual symptoms

These then are the known factors with which we must be concerned when we speculate regarding the etiology of cholecystitis Perhaps any one or more may initiate early changes in the mucosa with disturbance of function and the production of the symptoms with which we have become familiar

The most frequent cause of symptoms in gall bladder disease is the presence of stones What causes their formation? Do they result from the disturbance of function produced by a preexisting cholecystitis either acute or chronic or does the cholecystitis result secondary to the formation of stones? The answer to these questions is not clear In all probability both sequences occur

Disturbance of metabolism certainly promotes the formation of stones without cholecystitis necessarily being present previously About 10 per cent of all gall stones are found to be purely cholesterol and are believed to be the result solely of disturbed cholesterol metabolism The incidence of gall stones is higher among patients with hemolytic anemia (43%) and diabetes (30 2%) in portal cirrhosis and duodenal or gastric ulcers [4]

It seems probable however that the majority of instances of gall stones occur in gall bladders the function of which has been disturbed from infection or stasis of bile from some of the causes mentioned above A carefully recorded history will often reveal that mild digestive disturbance or jaundice occurred years before the appearance of symptoms signalling the presence of stones While we usually suppose that cholelithiasis may develop gradually over a period of years it is known that stones may form in a period of a few weeks or months Illustrative of this time

the contents or walls of diseased gall bladders less frequently than one would expect if direct invasion of bacteria is assumed to be a principal cause of either acute or chronic cholecystitis It is observed however that acute cholecystitis or recurrent attacks of chronic cholecystitis frequently follow closely after acute systemic infections [3] such as of respiratory prostatic or genito urinary origin Typhoid fever when prevalent was regarded as a highly potential precurser of cholecystitis and the typhoid organism has repeatedly been isolated from the bile gall bladder wall and from gall stones

Stasis of bile in the gall bladder is regarded as a very likely cause for irritation or chemical inflammation of the mucosa which may lead to poor absorption disturbed function infection and stone formation This stasis may result from many causes such as spasm or constriction of the sphincter of Oddi resulting from nervous stress fatigue pancreatic disease changes in intra abdominal pressure in the course of pregnancy abdominal tumors obesity drug effects notably opiates and histamine which are known to increase the tone of sphincter of Oddi and result in increased pressure within the gall bladder

Allergic reactions to infection drugs foods and environment have been suspected and in some instances proven to be a factor in the disturbance of gall bladder function This probably results from thickening and edema of the mucosa

Emptying of the gall bladder occurs in the normal individual several times every day with the intake of food Principally fats but to a less degree proteins and peptones upon entering the duodenum release cholecystokinin which stimulates normal emptying of the gall bladder Prolonged fasting or omission of fats from the diet may result in stasis and thereby promote changes within the mucosa leading to permanent impairment of function and cholecystitis acute or chronic These conditions prevail in post operative periods and in prolonged debilitating illnesses This factor as much as the typhoid bacillus itself may have been the basis for any causal relation between typhoid fever and gall bladder disease during that period when prolonged starvation was the accepted form of treatment for that disease

well contracted gall bladder with decrease in density of the shadow sometimes reveals stones not otherwise shown In a few instances a film on the following day has also shown a fainter shadow and outlined stones not shown during the routine test Occasionally also the cystic duct is better outlined following the fatty meal than previously Dr Lester R Whittaker has discussed this matter convincingly

The management of patients with a diagnosis of chronic cholecystitis with or without stones presents problems upon which there is much general agreement but still considerable divergence of opinion dependent upon one s teaching and personal experience Since these patients are frequently middle aged or beyond due consideration should first be given to other possible disease states such as diabetes blood dyscrasias cardiovascular or urinary tract disease which may either present confusing symptoms or else influence the plan of therapy Having determined that treatment should be directed principally toward the gallbladder disease surgical or medical regimen must be selected

Surgery is not generally urged at once except when stones are demonstrated or presumed to be present unless of course it be for complications such as empyema or suspected perforation or malignancy There are those who feel that surgery should be advised for all instances of cholelithiasis whether or not symptoms have been or are present This position we have never taken upon the assumption that the fear of complications as perforation malignancy empyema obstruction are not to be anticipated in a very high percentage of symptomless cholelithiasis Moreover complications following surgery are not unknown We have had a few instances of severe and prolonged complications following elective simple cholecystectomy which have tempered our enthusiasm with caution We usually discuss the problems and potential complications of gallstones frankly and thoroughly with the patient and tell him to let us know when he wishes to have cholecystectomy They usually do within a year

In the instance of a nonfunctioning gallbladder in which stones are not demonstrated dietary instructions are given and usually

factor is one patient under our observation on whom we have five cholecystograms in one year taken in three different x ray laboratories While the films seemed to be of equal clarity it was only with the last examination that stones were visualized Cholecystectomy resulted in complete relief of symptoms We felt sure that the formation of stones occurred during that year

It is our belief that infection and stasis with resulting mucosal changes precede and initiate the formation of stones in the large majority of patients with cholelithiasis

Upon what findings may we establish a diagnosis of cholecystitis? The symptoms and signs enumerated earlier constitute the principal guides to be obtained from history and physical findings Laboratory tests are of little help except as inflammation may be indicated by an increased leukocyte count The characteristics of the bile obtained by duodenal drainage is of considerable help We put great reliance on cholecystography perhaps we rely upon it too heavily It is a mistake to tell a patient that he has a normal gall bladder because the cholecystogram reveals good function and does not show stones Better to say only that this test is normal We believe a perfectly normal cholecystogram may sometimes be obtained in the presence of actual disease of the gall bladder—cholecystitis to be exact

It is likewise an error to base a diagnosis and advise surgery entirely upon a single cholecystogram which shows *nonfunction* but no stones Unless strongly supported by symptoms and other signs the test should be repeated at least once since poor absorption of the dye or other factors may yield a positive test occasionally and upon repetition excellent function be observed

Many roentgenologists have abandoned the routine use of the fat meal in the cholecystogram upon the asumption that evidence of good emptying of the gall bladder is not essential in the proof of a normally functioning organ This we believe to be generally a mistake All the information that we can obtain in the study of the gall bladder and its function is never too much Whether or not the gall bladder contracts well after ingestion of fat we believe to be valuable information regarding function A

toms or attention to the always perplexing post cholecystectomy syndrome

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one of the bile salt preparations is prescribed to be taken after meals Re evaluation of the gallbladder, including cholecystogram is advised in 3 to 6 months With better attention to diet and bowel function and the stimulating effect of bile salts to which is sometimes added a sedative digestive mixture there often is an improvement especially if the symptoms are mild or moderate at the beginning If a repeat cholecystogram again reveals a nonfunctioning gallbladder with or without stones and a general re evaluation confirms the orginal impression that chronic cholecystitis is most probably the basis of the patients symptoms we presume that stones are present and advise surgery

Since fat and protein seem essential for good gallbladder function it would seem unrealistic to withold these foods or limit them sharply for a patient with gallbladder disease Consequently our idea of dietary treatment is to encourage a well balanced diet limiting fats only because of obesity high blood cholesterol or other good reasons The patient is advised to observe regularity and moderation in eating and to omit such foods as he has found to disagree with him or to which he has a known intolerance Good bowel habits are also an objective The correction of any sources of infection such as bad teeth sinusitis prostatitis is sought

Mild anxiety states or plain nervousness and fear are allayed whenever possible as one adjunct to therapy This includes of course freeing the mind from fear of cancer which is so often found to be a real factor

A complete x ray study of the intestinal tract and gastric analysis are done at the time of the orginal study and any variations from normal as gastric or duodenal ulcer hiatus hernia pyloro spasm diverticula are given appropriate attention as well as of course any other systemic disease which may be present

To keep the patient s confidence and interest for a prolonged period of observation and sometimes uncertainity is not always possible It has been rewarding on a few occasions however to have them return after having ill advised surgery elsewhere to seek further advice for the continuation or recurrence of symp

that the figures I shall show you indicate the importance of biliary dyskinesia and the necessity for a continuance of this trial I hope also that they will encourage other workers to carry out similar studies

It is at present impossible on purely clinical grounds to make a diagnosis of biliary dyskinesia and to differentiate between a functional and morphological disorder of the biliary system The differentiation can only be made by using one or more of the an cillary methods of investigation These methods may be divided into two main groups

(1) The pre operative methods

(2) The per-operative methods

The usual technical investigation to clarify a diagnosis of biliary tract disorder is cholecystography but this examination in its classical or standard form is inadequate to diagnose a dyskinesia with accuracy and I have abandoned its use in favour of serial cholecystography a method by which the evacuation character istics of the gallbladder may be investigated Boyden in his orig inal work studied the evacuation of the normal gallbladder in response to the ingestion of food and drew an evacuation curve He seems to have deterred later investigators by the last para graph of his work But since it takes several hours to x ray the patient and several additional hours to make accurate tracings for each series a total of ten to fifteen hours work is required for each series a circumstance which would seem to preclude its use as a clinical method Since then his technique has been modified by Geraldo Siffert in 1949 by Busson in 1951 and Bugiel and Olivier in 1952 and finally Guy Albot and his collaborators simplified the procedure and with Toulet described the modern and much simpler method of serial cholecystography which I have followed

THE METHOD

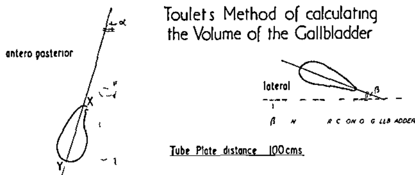
The patient is given a single does of Telepaque® the night be fore the examination and arrives in the radiological department 14 hours later With the patient in the supine position antero posterior and lateral views are taken and the plates developed

NEWER METHODS OF DIAGNOSIS AND TREATMENT OF BILIARY DYSKINESIA

J Dudfield Rose, M B B S F R C S *

About six years ago I became dissatisfied with the results of cholecystectomy and began a study of the unsatisfactory results following this operation by attempting to establish the incidence of failure I followed up 100 cases which were as nearly as possible consecutive on whom I had performed a cholecystectomy and found that 66 of the results were satisfactory and 34 were not Of these 34 patients 15 complained of symptoms as severe or more severe than those which they suffered before their operation A search for the possible causes of failure led me eventually to a study of biliary dyskinesia Biliary dyskinesia is regarded with scepticism by most clinicians in the United Kingdom in spite of the considerable amount of work done on this subject by continental and American investigators In spite of this scepticism I decided to carry out a thorough clinical trial of the methods of diagnosis and treatment of functional disorders of the biliary tract In this paper I propose to describe to you the methods I have used in the diagnosis and treatment of 300 consecutive patients suffering from disorders of the biliary and pancreatic systems who were investigated and treated in my clinic between September 1954 and February 1958 and to analyse my results As the number of cases when broken down into diagnostic groups is small and as the length of follow up is not more than four years I hesitate to draw any dogmatic conclusions but I believe

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$$\text{VOLUME} = \frac{\text{area antero posterior} \times \text{area lateral}}{\text{length } X\,Y} \times K$$

K 0 5 … $< 40^\circ$
0 62 … 40° 45°
0 75 … $> 45^\circ$

Fig 1 Toulets Method of computing the volume of the gallbladder Areas of the gallbladder shadows are measured either by using a planimeter or tracing the shadow on to squared paper

cause there is an obstruction to its outlet such as a fibrosed cystic duct or a spasm of the sphincter of Lutkens or on the other hand the gallbladder may be atonic These two types of stasis may be differentiated by studying the angle of erection This angle is dependent on the tone and force of contraction of the gallbladder and the resistance to its evacuation If there is an obstruction there will be an increase in the tone of the gallbladder and an increase in the force of contraction in such a condition the initial angle of erection will be high and the increase in this angle will be greater than normal even rising to 90 (Fig 5) It is impossible by this method to differentiate between a gross primary atony the cholecystatony of Chiray & Pavel and a secondary atony resulting from a long standing obstruction The final diagnosis can be made at operation

The initial volume of the gallbladder may be small less than 20 ccs as occurs in some cases of hypotonia in spasm or fibrosis

immediately If the gallbladder has concentrated the dye sufficiently and there is no morphological abnormality which in itself would indicate an operation the patient is then given 100 ccs of ice cold normal saline to drink after which he lies in the prone position for five minutes Then he is given the standard fatty meal (2 eggs beaten up in half a pint of milk) and turned to the supine position Ten minutes later antero posterior and lateral plates are taken and these are repeated at twenty thirty and eighty minutes When the plates are developed and dry the gallbladder shadows are traced out on paper and the volume computed by Toulet s method (Fig 1) In addition the angle of erection of the gallbladder (i e the angle between the long axis of the gallbladder and the long axis of the spine in the lateral view) is measured Two curves are then drawn one an evacuation curve and the other a curve of the angle of erection (Fig 2) From a study of these two curves a diagnosis is made

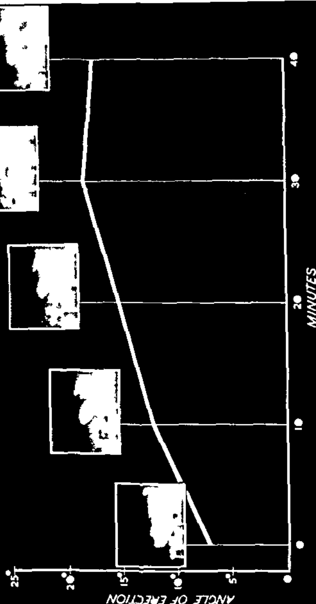
NORMAL PHYSIOLOGICAL CHANGES DURING THE TEST

After the ingestion of the fatty meal the shadow of the gallbladder becomes smaller and in the antero posterior view moves proximally and rotates externally In the lateral view the shadow rotates around a point somewhere in the infundibulo cystic region so that the long axis becomes more vertical and the angle of erection which is normally 5° to 15 increases between 5 to 15° and at the same time the shadow as a whole approaches the anterior abdominal wall

The normal volume of the gallbladder is about 25 ccs and the decrease in volume after a fatty meal is normally about 30% in the first five minutes and 70% in the first thirty minutes

ABNORMAL STATES

A gallbladder may evacuate abnormally either by doing so insufficiently hypokinesia (Fig 3) or too rapidly hyperkinesia (Fig 4) In hypokinetic states there is said to be a vesicular stasis In my series there were 57 patients who were shown to have a vesicular stasis and 15 patients had a vesicular hyperkinesia The gallbladder may evacuate insufficiently either be



(b) The curve of the angles of erection

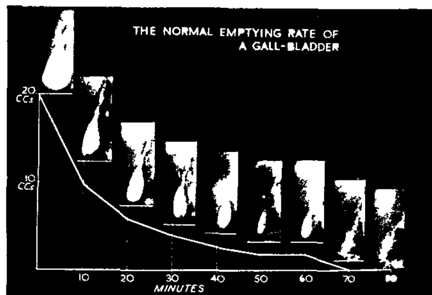


Fig 2 (a) The evacuation curve of a normally functioning gallbladder

of the gallbladder A large gallbladder of more than 40 ccs is found in some conditions of hypotonic stasis and very large gall bladders of 70 100 ccs occur in the last stages of asystole behind an almost complete cystic obstruction of long duration

A more accurate but much more time consuming method which requires a considerable degree of skill and experience in the interpretation of the findings is the trans parieto hepatic vesicular puncture described by Kapandji in 1950 Having no great experience of this method I will only outline the technique The patient is prepared as for a cholecystogram and if the gallbladder is visible on radioscopy a needle is inserted under the screen through the skin and liver into the gallbladder This needle is attached to a manometer and reservoir of Diodone® A series of pressure readings is recorded and a series of radiographs taken It is a complicated and lengthy procedure but from a study of the various pressures recorded and the radiographs taken at those pressures it is possible to form a complete concept of the working not only of the biliary tract and its sphincters but also of the duodenal sphincters which are closely inter related

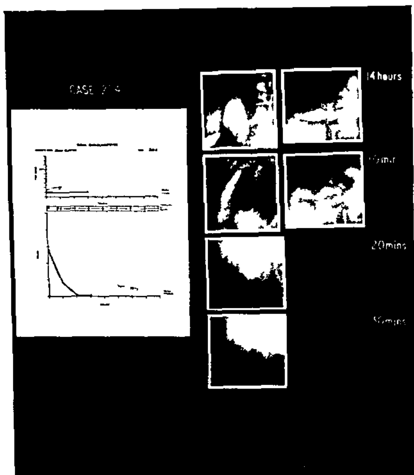


Fig 4 Serial cholecystogram of hypotonic vesicular hyperkinesia The gallbladder is of normal size and evacuates more rapidly than normal and there is no increase in the angle of erection during the test

storage of bile the sphincter of Oddi is contracted and the gall bladder relaxes and that during the discharge of bile the gall bladder contracts and the sphincter is relaxed Two years later Lyon using this principle evolved the non surgical drainage of the gallbladder" and from this the Meltzer Lyon Test was devel oped In 1948 Varela Lopez Varela Fuente and Martinez Prado pointed out that this test though more informative than a chole

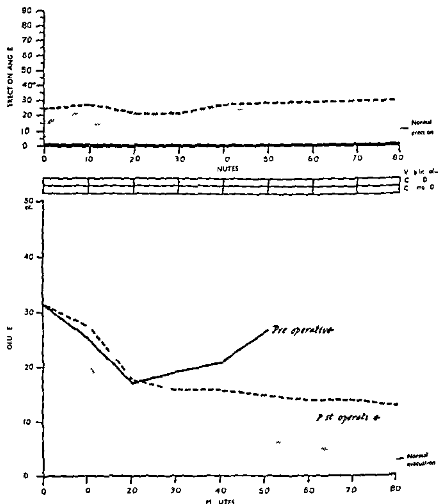


Fig 3 Serial cholecystogram of a hypotonic vesicular stasis The gall bladder is of normal size and begins to evacuate at an insufficient rate and then fills up again The angle of erection is 0 and remains so throughout the test (The shaded areas on the graph indicate normal limits)

In the absence of the gallbladder shadow due either to its removal or exclusion the investigator may resort to the chrono volumetric estimation of bile This test is the outcome of the earlier work of Meltzer who in 1917 pointed out that during the

collected in the common duct It is a golden yellow colour slightly viscous with a bilirubin content of 6 13 mgms% Having obtained a sample of this common duct bile during the first period of the test 40 ccs of warm olive oil are injected down the tube and the prompt result is the cessation of biliary flow due to closure of the sphincter of Oddi constituting the second period After about 3 minutes the third period begins during which time the sphincter opens and about 2 5 ccs of clear yellow bile A flows for 2 to 6 minutes The fourth period begins when the clear yellow bile changes to darker bile "B This is a more concentrated brown coloured bile which flows slowly and uniformly from the gallbladder for a period of about 20 minutes It measures about 30 ccs in amount and has a bilirubin content of 40 70 mgms% The end of this fourth or vesicular period is signalled by the flow of a clear yellow bile C which is bile which has recently been secreted by the liver cells and is slowly flowing down the ducts and this final or fifth period lasts as long as the tube remains in position

A second and stronger stimulus in the form of 30 ccs of 30% magnesium sulphate may be given if considered necessary During the test the patient should experience no abnormal sensations In patients who have had the gallbladder removed or in whom it is excluded by stones or disease two of these periods are absent the third and fourth The first two and the last periods are the same

Many anomalies have been described and from an understanding of these the authors of this technique claim that a very accurate assessment of biliary function may be obtained Briefly functional disturbances of the gallbladder cause abnormalities to appear in the vesicular period which may be either shortened or prolonged and the bile "B may be more concentrated than normal Functional disturbances of the common duct and its sphincter alter significantly the first three periods and most important are changes in the length of time the sphincter of Oddi remains closed

In 1952 and 1954 Guy Albot drew attention to some possible fallacies in the test and its interpretation and demonstrated that

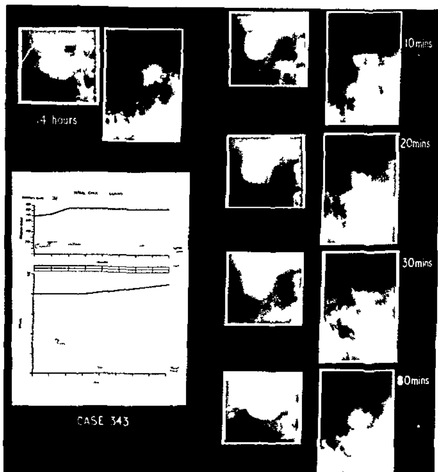


Fig 5 Serial cholecystogram of hypertonic vesicular stasis The gallbladder is slightly larger than normal and does not evacuate at all the angle of erection approaches 90 The antero posterior views at 10 20 and 30 minutes show the typical golf ball gallbladder

cystogram gave little or no information concerning the functioning of the sphincters and they introduced the time factor

The test is carried out very similarly to the Meltzer Lyon Test A duodenal tube is passed on the fasting patient and shortly after the tube enters the duodenum a bilious fluid begins to flow and is collected by suction in bottles which are changed at intervals of five minutes The first sample consists of bile which has

collected in the common duct It is a golden yellow colour slightly viscous with a bilirubin content of 6 13 mgms% Having obtained a sample of this common duct bile during the first period of the test 40 ccs of warm olive oil are injected down the tube and the prompt result is the cessation of biliary flow due to closure of the sphincter of Oddi constituting the second period After about 3 minutes the third period begins during which time the sphincter opens and about 2 5 ccs of clear yellow bile A flows for 2 to 6 minutes The fourth period begins when the clear yellow bile changes to darker bile B This is a more concentrated brown coloured bile which flows slowly and uniformly from the gallbladder for a period of about 20 minutes It measures about 30 ccs in amount and has a bilirubin content of 40-70 mgms% The end of this fourth or vesicular period is signalled by the flow of a clear yellow bile C which is bile which has recently been secreted by the liver cells and is slowly flowing down the ducts and this final or fifth period lasts as long as the tube remains in position

A second and stronger stimulus in the form of 30 ccs of 30% magnesium sulphate may be given if considered necessary During the test the patient should experience no abnormal sensations In patients who have had the gallbladder removed or in whom it is excluded by stones or disease two of these periods are absent the third and fourth The first two and the last periods are the same

Many anomalies have been described and from an understanding of these the authors of this technique claim that a very accurate assessment of biliary function may be obtained Briefly functional disturbances of the gallbladder cause abnormalities to appear in the vesicular period which may be either shortened or prolonged and the bile B may be more concentrated than normal Functional disturbances of the common duct and its sphincter alter significantly the first three periods and most important are changes in the length of time the sphincter of Oddi remains closed

In 1952 and 1954 Guy Albot drew attention to some possible fallacies in the test and its interpretation and demonstrated that

too great a reliance cannot be placed on this form of investigation but as already stated in the absence of a gallbladder shadow it is the only method at present available which can give information concerning abnormalities of biliary tract function

Having made a pre operative diagnosis with the help of one or more of the methods of investigation described the clinician decides whether an operation is indicated Should an operation be considered necessary then the type of operation to be performed is finally decided by the result of per operative manometry and radiology

Heidenhain working in Breslau in 1868 first measured the pressure within the biliary tract In 1888 Oddi attributed this pressure to the tone of the sphincter which now bears his name Since those early days there have been many workers who like Herring and Simpson in 1907 studied the pressure of bile secretion Judd and Mann in 1917 and Potter and Mann in 1926 who studied pressure changes within the tract MacGowan Butch and Walters in 1936 who studied biliary tract pressure in relation to pain and Doubilet and Colp in the following year who studied the resistance of the sphincter of Oddi In 1918 Reich accidentally demonstrated the biliary tract radiologically after which many attempts were made but it was not until 1931 that Mirizzi of Cordoba took a most important step by showing the possibility of demonstrating the bile ducts during operation and in 1947 McNeil Love in England was stressing its importance In the early days of the war (1940) Caroli devised a method of combining these two investigations and two years later Mallet Guy simplified the technique and reduced the time taken This later method while not giving quite as much detailed information as Caroli's saves a considerable amount of time and gives all the information necessary to control the type of operation to be carried out

The investigation is divided into two parts which follow immediately one after the other The first is to measure the pressure within the biliary tract and the other is to take a cholangiogram The type of anaesthesia is of prime importance and there must be

no deviation from it Experimentally it has been found that the pressure within the biliary tract in a patient under surgical anaesthesia produced by nitrous oxide oxygen and ether given by means of a closed circuit and without any form of premedication whatever is the same as in the conscious patient Any drug which acts on the sympathetic or para sympathetic nervous systems must be avoided nor can relaxants be allowed

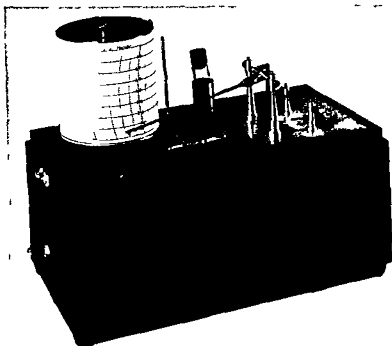


Fig 6 The recording manometer

The pressures are recorded on a manometer which resembles the recording barograph only the drum revolves once in thirty seconds (Fig 6) The pressure capsule is connected to a canula inserted into the gallbladder or common duct by a long tube which rises from the patient to about three feet before descending to the manometer Inserted in this tube about a foot from the canula is a "T" junction leading to a two way syringe fitted with inlet and outlet valves (Fig 7) When estimating the pressure

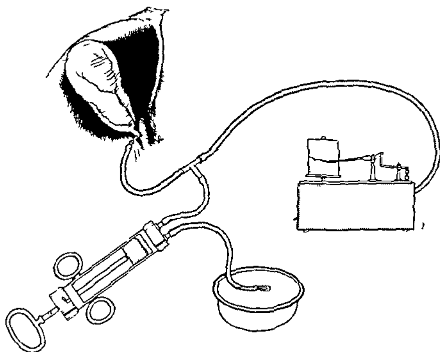


Fig 7 The disposition of the manometer syringe and canula

about 5 ccs of isotonic saline at body temperature are injected into the system this causes the manometer pen to rise sharply at the end of the injection the pen falls rapidly at first and then more slowly as the pressure stabilizes at a lower level The manoeuvre is repeated several times until successive pressures stabilize at approximately the same level The final stabilized pressure is the pressure which the sphincter of Lutkens (if the canula is inserted into the gallbladder) or the sphincter of Oddi (if the canula is in the common duct) will support The normal pressure within the gallbladder is 18 cms and the normal pressure within the common duct is between 8 and 14 cms Having recorded these pressures the cholangiograms are taken Fluid Lipiodol® may be used but this medium is extremely radio opaque and will obscure small stones On account of this fact some workers use a weak solution of Diodone® High concentrations of water soluble iodine preparations are irritating to the

ducts so a percentage of not more than 25% is advisable

The technique is to inject 20 ccs of Diodone® into the gall bladder and take a radiograph then the injection is repeated and a second picture is taken after two or three minutes a final picture shows the degree of emptying which has taken place in that time From a study of the pressure curves information concerning the tone of the sphincters is obtained or the presence of an obstructive lesion is demonstrated The radiographs will show morphological abnormalities of the biliary tract and from these findings the type of operation is indicated

I have described the techniques used in the diagnosis of biliary dyskinesia and I shall now attempt to demonstrate the application of these methods to describe the treatment of dyskinesia and to give you a statistical analysis of the results obtained from that treatment

The first step in the diagnosis is the recognition of a pattern of dyspepsia which points to a tentative diagnosis of biliary tract disorder As I have already stated at present it is impossible to diagnose a dyskinesia from a clinical history and physical examination alone The next step therefore is to attempt to confirm the diagnosis of a biliary tract disorder and to clarify further that diagnosis by some technical or laboratory investigation The investigation of choice is the cholecystogram Cholecystography will demonstrate whether the gallbladder will concentrate the dye sufficiently to cast a shadow or not If the gallbladder does not cast a shadow I regard that as abnormal and should the symptoms be of sufficient severity an indication for operation If a shadow is present it may show some morphological abnormality which is sufficient indication for operative interference If such an abnormality is not present serial studies are carried out The decision to operate is taken after consideration of the cholecystographic report together with the clinical and any other laboratory findings

The indications for treatment which I have observed are finally determined by per operative manometry and radiology They are quite broadly (1) to remove any disease focus (2) to remove or by pass any organic obstruction (3) to correct any bil

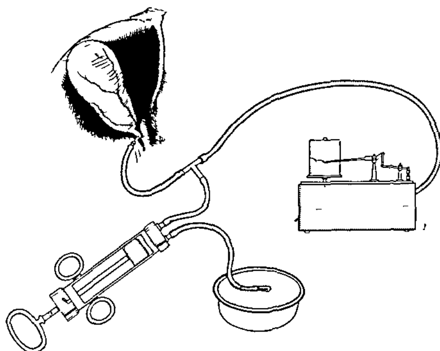


Fig 7 The disposition of the manometer syringe and canula

about 5 ccs of isotonic saline at body temperature are injected into the system this causes the manometer pen to rise sharply at the end of the injection the pen falls rapidly at first and then more slowly as the pressure stabilizes at a lower level The manoeuvre is repeated several times until successive pressures stabilize at approximately the same level The final stabilized pressure is the pressure which the sphincter of Lutkens (if the canula is inserted into the gallbladder) or the sphincter of Oddi (if the canula is in the common duct) will support The normal pressure within the gallbladder is 18 cms and the normal pressure within the common duct is between 8 and 14 cms Having recorded these pressures the cholangiograms are taken Fluid Lipiodol® may be used but this medium is extremely radio opaque and will obscure small stones On account of this fact some workers use a weak solution of Diodone® High concentrations of water soluble iodine preparations are irritating to the

tion revealed tenderness below the right costal margin The biochemical examination of blood serum showed no abnormality Serial cholecystogram 9 11 55 The gallbladder evacuated insufficiently and the angle of erection did not rise throughout the test (Fig 3) A provisional diagnosis of hypotonic vesicular stasis was made Operation 30 11 55 An elongated flabby gall bladder was found The pressure when measured in the gall bladder stabilized at 15 cms of water (Fig 8) A right greater splanchnicectomy was performed

Result After almost three years the patient is completely cured A repeat serial cholecystogram showed an improvement in the evacuation characteristics of the gallbladder

There were 13 cases in which no abnormality other than a hypotonia was demonstrated and on whom only a right splanchnicectomy was performed Table I shows a detailed analysis of the results from which it may be concluded that 12 patients had a satisfactory result and one did not

A vesicular stasis may however be due to an obstruction to evacuation which can be organic spasmodic or a combination of the two A classic example of this hypertonic type of vesicular stasis in which serial cholecystography shows a high or rising angle of erection is

Case No 343 L H Male Aged 54

The patient had complained of dyspepsia for as long as he could remember his main symptoms were an epigastric and right subcostal ache aggravated by foods especially fats and associated with flatulence post prandial fullness and abdominal swelling Physical examination revealed right subcostal tenderness The biochemical examination of his blood serum showed no abnormality He had been investigated in hospital several times prior to admission to my clinic His barium meal showed no abnormality and a classical cholecystogram was reported as being normal A diagnosis of hiatus hernia was made and the patient was waiting for an operation on this diagnosis Serial

ary dyskinesia In cases of hypotonia I perform a right splanchnicectomy In hypertonia due to a spasm I do a low vagotomy on the lesser curvature of the stomach These operations are based on the considerable amount of experimental and clinical evidence produced by Mallet Guy and his collaborators in 1941 1942 and 1953 when he showed that the right greater splanchnic nerve is the inhibitor and the left vagus the motor nerve of the biliary tract I shall also analyse the results of such treatment *in the more important clinical groups I regret space does not* permit a complete analysis of all cases

Each patient was followed up by interview one two three six and twelve months after operation and thereafter annually The *results are classified in the following manner*

Group Ia No symptoms no dietary restrictions
Group Ib No symptoms but some dietary restrictions
Group II Persistence of minor symptoms i e symptons less severe than before operation (the presence of even one symptom puts the patient into this group)
Group III Persistence of major symptoms i e symptoms as severe or more severe than before operation (the presence of even one symptom puts the patient into this group)
Group IV Recurrence after a period of relief

Out of 300 consecutive patients suffering from a biliary tract disorder investigated and treated 72 showed an abnormal serial cholecystogram (it may be noted in parenthesis that these patients showed no abnormality on "classical cholecystography) The commonest abnormality was a vesicular stasis indicated by an insufficient evacuation curve There were 57 such cases A classical example of a hypotonic biliary vesicular stasis was

Case No 107 R B Female Aged 57

The patient gave a three year history of right subcostal pain radiating to the chest and back She had headaches associated with a flatulent dyspepsia fullness after meals nausea and vomiting The dyspepsia was aggravated by fats Physical examina

TABLE I

HYPOTONIC VESICULAR STASIS

13 PATIENTS FOLLOWED UP FOR MORE THAN 3 MONTHS

DURATION OF FOLLOW UP	CLASSIFICATION OF RESULTS				
	I	Ib	II	III	IV
THREE MONTHS	1				
THREE TO SIX MONTHS	1				
SIX MONTHS TO ONE YEAR			1	1	
ONE TO TWO YEARS	4	1	1		
TWO TO THREE YEARS	3				
	9	1	2	1	
	12				

GOOD RESULTS 12

BAD RESULTS 1

cholecystogram 22.4.58 demonstrated an almost complete obstruction and a very high angle of erection.

Operation 16.5.58. There were adhesions between the neck of the gallbladder and the surrounding viscera. The stabilised pressure taken within the gallbladder rose to 26 and fell to 17. The cholecysto-cholangiogram showed a well marked obstruction in the infundibulo-colic region. The common duct showed no abnormality. Pressures taken within the common duct stabilised at 4 cms of water. A cholecystectomy and right splanchnicectomy were performed. Pathological examination showed an almost complete block at the junction between the neck and the infundibulum of the gallbladder.

Result. A complete cure after three months.

Table II shows the analysis of the results obtained in these cases of hypertonic vesicular stasis. There were 17 such cases (one patient being admitted twice) and 16 patients could be considered as having satisfactory results and 1 as unsatisfactory. An interesting example of biliary hypertonia was diagnosed at operation by manometry.

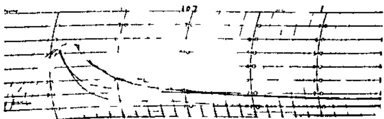


Fig 8 *Case No 107* The graph shows the stabilisation of the intra vesicular pressures at 15 cms of water The radiograph demonstrates a hypotonic gallbladder and a common duct which has a gentle curve to about a right angle

TABLE II

HYPERTONIC VESICULAR STASIS

18 PATIENTS FOLLOWED UP FOR MORE THAN THREE MONTHS
(1 PATIENT ADMITTED TWICE)

DURATION OF FOLLOW UP	CLASSIFICATION OF RESULTS				
	I	Ib	II	III	IV
THREE MONTHS			1		
THREE TO SIX MONTHS	1	2	1		
SIX MONTHS TO ONE YEAR	4		4		1
ONE TO TWO YEARS	1	2			
TWO TO THREE YEARS					
	6	4	6		
	16				

GOOD RESULTS 16

BAD RESULTS 1

Case No 345 A H Female Aged 45

There was a history of dyspepsia for 6 years at the onset of which a barium meal and cholecystogram were negative One year prior to admission to hospital she had a transient attack of jaundice She complained of an acute gripping pain below the right costal margin and in the epigastrium which radiated to both shoulders and to the lower abdomen There was flatulence and nausea She had a progressive jaundice which during her stay in hospital became associated with fever On Examination she was deeply jaundiced with tenderness below the right costal margin The blood serum analysis showed a direct Van den Bergh reaction the alkaline phosphatase was 36 4 A pancreatic efficiency test showed a reaction very suggestive of a carcinoma and a duodenography showed a large malignant ulcer in the second part of the duodenum (Fig 10) Cytology of the duodenal juice revealed malignant cells

Operation 19 5 58 The gallbladder was large and tense and somewhat inflamed the head of the pancreas was hard and the

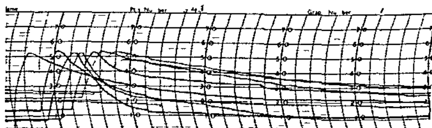


Fig 9 *Case No 343* The graph shows that the stabilised intravesicular pressures rose to 26 cms and then fell to 17 cms of water The cholecysto cholangiogram demonstrates quite clearly the infundibulo colic kink



Fig 12 *Case No 204* The graph shows an abnormally low stabilised intra vesicular pressure of 8 cms of water The radiograph demonstrates a pyriform atonic gallbladder with a dilated cystic duct and a long sinuous common duct

liver showed multiple very small abscesses The pressure within the gallbladder rose to 38 cms of water the cholecystocholangiogram showed a very large reflux into a greatly dilated hepatic duct system a dilated common duct which terminated in an irregular concave amputation (Fig 11) The gallbladder was removed and the pressure within the common duct stabilised at 24 cms of water At this stage the patient s general condition did not warrant an attempt to proceed further consideration being given especially to the multiple cholangitic abscesses in the liver The common duct was therefore drained via the cystic duct The patient made a good recovery A combined duodenogram and cholangiogram showed the blocked common duct and the malignant ulcer

Operation 2 7 58 A duodeno-pancreatectomy was performed from which the patient has made a complete recovery

Serial cholecystography may demonstrate the opposite condition—a vesicular hyperkinesia in which the gallbladder evacuates more rapidly than normal This condition was described by Pallard in 1923 Chiray and Lomon in 1925 and by Berard and Mallet Guy in 1928 A vesicular hyperkinesia may be purely functional or it may be associated with other pathological conditions such as a spasmodic colon duodenitis or ulcer chronic appendicitis and chronic cholecystitis

A typical example of this condition is

Case No 204 J C Female Aged 67

There was a 12 year history of abdominal pain below the right costal margin radiating to both shoulders and chest associated with severe headache flatulence fullness after meals and nausea The dyspepsia was aggravated by fats Physical examination revealed tenderness below the right costal margin Biochemical examination of the blood serum showed no abnormality

Serial cholecystogram 1 8 56 showed a vesicular hyperkinesia with a hypotonia (Fig 4)

Operation 7 1 57 The pressure within the gallbladder stabilised at 8 cms of water The cholecystocholangiogram showed nothing abnormal (Fig 12) A right splanchnicectomy was performed

TABLE IV

CHOLECYSTECTOMY IN CASES WITH HYPOTONIA WITHOUT SPLANCHNICECTOMY

31 CASES FOLLOWED UP FOR MORE THAN THREE MONTHS

DURATION OF FOLLOW UP	CLASSIFICATIO OF RESULTS				
	Ia	Ib	II	III	IV
THREE MONTHS		3	3	1	
THREE TO SIX MONTHS			4		
SIX MONTHS TO ONE YEAR	4	2	1		
ONE TO TWO YEARS	1	1	2		3
TWO TO THREE YEARS	2	1	-	1	
	7	7	12	2	3
	26			5	

GOOD RESULTS 26

BAD RESULTS 5

nesia I shall review the results of cholecystectomy carried out on patients who had a hypotonic dyskinesia in addition to some morphological abnormality These cases were divided into two groups in one a cholecystectomy only was performed and in the other a cholescystectomy and right greater splanchnicectomy were performed The following Tables IV V and VI set out the results While the figures are not at present large nor is the fol low up longer than four years they indicate that a failure to diag nose and treat a hypotonic dyskinesia resulted not only in a greater number of bad results but also a smaller proportion of complete cures

I have cited several examples of the two types of biliary dyski nesia Hypotonia is the commoner of the two and was present in 143 cases 33 of which were unassociated with any morpho logical abnormality Table VII shows a statistical analysis of these cases There were 67 examples of hypertonia of which only 9 were due to pure spasm and there were 7 which were associated with malignant disease These figures demonstrate the compara

Result The patient was considerably improved and a repeat cholecystogram showed an improvement in the evacuation curve

There were 15 patients in this group only 5 of whom had a pure hypotonia 2 had a chronic cholecystitis one had a duodenal ulcer one had a gallstone one was hypertonic one had appendicitis and 3 had an infundibulo colic kink and one was not submitted to operation

An analysis of the results obtained showed that of the 14 patients who were treated surgically 13 had satisfactory results and one had a bad result Table III shows the complete analysis of

TABLE III

VESICULAR HYPERKINESIA

15 PATIENTS FOLLOWED UP FOR MORE THAN THREE MONTHS
(1 PATIENT NOT SUBMITTED TO OPERATION)

DURATION OF FOLLOW UP	CLASSIFICATION OF RESULTS				
	Ia	Ib	II	III	IV
THREE MONTHS		1	1		
THREE TO SIX MONTHS		1	1		
SIX MONTHS TO ONE YEAR	2	1	3	1	
ONE TO TWO YEARS	1		2		
TWO TO THREE YEARS					
	3	3	7	1	
	13 (Ia–II)				

GOOD RESULTS 13

these results as judged by the criteria I have outlined

The incidence of dyskinesia in biliary tract disorders is high Out of 300 patients who form the basis of this review 201 were found to have a dyskinesia of which 47 had a pure dyskinesia unassociated *with any morphological abnormality It is however* important to take into account the dyskinesia which is associated with morphological abnormalities in the remaining 154 patients In order to demonstrate the importance of this associated dyski

TABLE VII

STATISTICAL ANALYSIS OF 143 CASES OF BILIARY HYPOTONIA

1 GALLSTONES			45
	STONES IN GALLBLADDER	43	
	STONES IN COMMON DUCT	2	
2 CHRONIC CHOLECYSTITIS			49
3 VESICULAR STASIS			41
	PURE HYPOTONIA	13	
	CHR CHOLECYSTITIS	8	
	VALVE OR KINK	1	
	STONE	2	
	DUODENAL ULCER	2	
	CHR PANCREATITIS	1	
	CYSTIC DUCT FIBROSIS	1	
4 VESICULAR HYPERKINESIA			10
	PURE HYPOTONIA	4	
	KINK	3	
	CHR CHOLECYSTITIS	2	
	DUODENAL ULCER	1	
5 POST CHOLECYSTECTOMY SYNDROME			2
	PURE HYPOTONIA	12	
	CHR PANCREATITIS	4	
	CHOLANGIO HEPATITIS	5	
	STONE IN COMMON DUCT	1	
6 POST GASTRECTOMY SYNDROME			4

Case No 73 G S Female Aged 40

Two years prior to admission a cholecystectomy was performed for gallstones following which the patient was symptom free for six months when she began to complain of pain below the right costal margin which spread across the upper abdomen and radiated to her chest and back She had a flatulent dyspepsia with nausea and daily severe migrainous headaches which were aggravated by fatty food Physical examination revealed tenderness below the right costal margin and biochemical examination of the blood serum showed no abnormality An intravenous cholangiogram showed no abnormality The chrono-volumetric estimation of bile was characteristic of a hypotonia of the sphincter of Oddi —immediate abundant flow of bile a very short period of closure of the sphincter of Oddi and a large flow of bile "A" after the sphincter opened

Operation 6 7 55 The cystic duct stump was cannulated and the pressure within the common duct stabilised at 2 cms of water The cholangiogram showed nothing abnormal (Fig 13) A right splanchnicectomy was performed

TABLE V

CHOLECYSTECTOMY IN CASES WITH HYPOTONIA WITH SPLANCHNICECTOMY

25 CASES FOLLOWED UP FOR MORE THAN THREE MONTHS

DURATION OF FOLLOW UP	CLASSIFICATION OF RESULTS				
	Ia	Ib	II	III	IV
THREE MONTHS	1	1	1		
THREE TO SIX MONTHS	1		1		
SIX MONTHS TO ONE YEAR	3	1	1		
ONE TO TWO YEARS	7		3		1
TWO TO THREE YEARS	3		1		
	15	2	7		1
	24				

GOOD RESULTS 24

BAD RESULTS 1

TABLE VI

RESULTS OF CHOLECYSTECTOMY WITH AND WITHOUT SPLANCHNICECTOMY IN CASES WITH A HYPOTONIA

OPERATION	I	Ib	II	III	IV	TOTAL
CHOLECYSTECTOMY ALONE	7	7	12	2	3	31
CHOLECYSTECTOMY & SPLANCHNICECTOMY	15		7	0	1	25
CHOLECYSTECTOMY ALONE	22 6%	22 6%	38 6%	6 5%	9 7%	
CHOLECYSTECTOMY & SPLANCHNICECTOMY	60 0%	8%	28		4	

tive rarity of spasmodic hypertonia Table VIII shows a statistical analysis of the cases of biliary hypertonia

I began this paper with a reference to failures and recurrences after cholecystectomy — termed rightly or wrongly the post cholecystectomy syndrome After blind cholecystectomy i e without per operative manometric and radiological control there is about 15% of failures There were 34 patients in this series who were investigated and treated surgically for a post cholecystectomy syndrome I shall describe three examples



Fig 13 *Case No* 73 The graph shows a low stabilised intra-duct pressure of 2 cms of water The radiograph shows a normal common duct with a widely open sphincter of Oddi

volumetric estimation of bile showed a normal time of closure of the sphincter of Oddi but an interrupted flow of a hyperconcen

TABLE VIII

STATISTICAL ANALYSIS OF 67 CASES OF BILIARY HYPERTONIA

A	MALIGNANT CASES				7
		MALIGNANT PANCREAS		4	
		MALIGNANT GALLBLADDER		1	
		MALIGNANT HEPATIC DUCT		1	
		MALIGNANT COMMON DUCT		1	
B	SIMPLE CASES				60
	1 GALLSTONES			31	
		GALLBLADDER	28		
		COMMON DUCT	17		
	2 CYSTIC VALVE OR KINK			11	
	3 PURE SPASM			9	
		SPASM OF SPHINCTER OF ODDI	7		
		SPASM OF SPHINCTER OF LUTKEN	2		
	4 CHRONIC CHOLECYSTITIS			2	
	5 FIBROSIS OF CYSTIC DUCT			2	
	6 FIBROSIS OF SPHINCTER OF ODDI			1	
	7 SPASM OF SPHINCTER OF LUTKENS DUODENAL ULCER			2	
	8 CHRONIC PANCREATITIS			1	
	9 ACUTE PANCREATITIS			1	

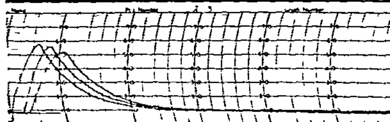
Result Complete disappearance of symptoms but patient restricts the fats in her diet

This is a classical example of a post cholecystectomy syndrome due to a pure hypotonic dyskinesia There were 9 such cases and an analysis of the results showed that all the cases could be considered satisfactory

There were only 3 cases of hypertonia one of which is an example of bilio duodenal dyskinesia

Case No 233 P C Female Aged 41

This patient had complained of dyspepsia for 12 years and 8 years prior to admission had a cholecystectomy for a non calculous cholecystitis and had some relief for about one year after which she complained of lower abdominal ache backache flatulence post prandial fullness nausea vomiting and abdominal swelling A prominent feature was a burning sensation in her eyes Physical examination revealed nothing abnormal the bio chemical examination of her blood serum was normal a barium meal and intravenous cholangiogram were normal The chrono



common duct opening above it Graph No 2 (b) taken after blocking the vagus shows that the pressure had fallen to 8 cms of water—a low normal and the radiograph shows that the spasm had disappeared.

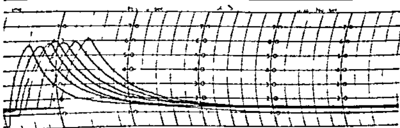


Fig 14 *Case No 233* The graph No 1 (a) shows that the pressure within the common duct stabilised at 14 cms of water—a high normal The radiograph shows a spasm of the medio-duodenal sphincter with a short

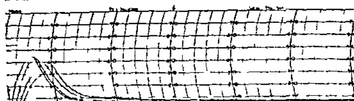


Fig 15 *Case No 146* The graph shows that the common duct pressure stabilised at 16 cms of water The radiograph shows an enormous dilatation of the common hepatic duct and an irregular lower end of the duct

trated bile A The interrupted flow of bile A was difficult to reconcile with the time of closure of the sphincter of Oddi

Operation 15 4 57 A fairly long cystic duct stump was cannulated and the pressure within the common duct stabilised at 15 cms of water The cholangiogram showed a short common duct which opened into the proximal portion of the 2nd part of the duodeum just below the opening there was a well marked spasm of the sphincter of Kapandji (i e the medio duodenal sphincter) (Fig 14a) The vagus was blocked on the lesser curve of the stomach with 1% Xylocaine and a further pressure reading was taken which stabilised at 8 cms of water A repeat cholangiogram showed that the duodenal spasm had disappeared (Fig 14b) The spasm accounted for the equivocal chronovolumetric estimation of bile

A low vagotomy was performed

Result The patient now states she is completely cured and has lost all her symptoms and can eat anything and states that she cannot remember every feeling so well in her life

Of the 3 patients who had a hypertonia all had satisfactory results after a low vagotomy

An example of organo functional dyskinesia is

Case No 146 M H Female Aged 60

The patient had complained of dyspepsia for as long as she could remember One year prior to admission she had a cholecystectomy for calculous cholecystitis and obtained some relief for three months after which her symptoms recurred She complained of epigastric pain which radiated to her back There was post prandial fullness nausea and vomiting and an intolerance of fats She had several attacks of jaundice and her urine became dark coloured during attacks of pain Physical examination revealed right subcostal tenderness The biochemical examination of her blood serum showed no abnormality An intravenous cholangiogram showed a very dilated common duct

Operation 8 5 56 The cystic duct stump was cannulated and the pressure within the common duct stabilised at 6 cms of water The cholangiogram showed an enormously dilated duct system

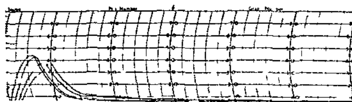


Fig 15 *Case No 146* The graph shows that the common duct pressure stabilised at 16 cms of water The radiograph shows an enormous dilatation of the common hepatic duct and an irregular lower end of the duct

with gross irregularity of the lower end of the duct (Fig 15) The head of the pancreas was hard and nodular A chronic capitular pancreatitis associated with a hypotonia was diagnosed A right splanchnicectomy was performed

Result The patient is symptom free and is able to eat anything

There were 8 cases in which an organo-functional cause was found and of these 7 patients had satisfactory results and one had an unsatisfactory result

TABLE IX

POST CHOLECYSTECTOMY SYNDROME

TOTAL NUMBER OF PATIENTS 34

			RESULTS		
			SATIS	UNSATIS	DIED
I	PURE DYSKINESIA	12			
	HYPOTONIA		9		
	HYPERTONIA		3		
II	ORGANO FUNCTIONAL	8			
	HYPOTONIA				
	( ) CHOLANGIO HEPATITIS		5		
	(b) CHR PANCREATITIS		2	1	
III	ORGANIC LESIONS	13			
	STONES		4		1
	CHR PANCREATITIS		4		1
	DUODENAL ULCER		1		
	CYSTIC DUCT STUMP			1	1
IV	N A D	1			

Table IX sets out an analysis of the diagnosis and results obtained in the 34 patients investigated and treated surgically for a post cholecystectomy syndrome 28 patients had satisfactory results two had unsatisfactory results three patients died (one from acute pancreatitis one from acute renal failure and the third from pneumonia and acute circulatory failure) and in one case no cause was found for the symptoms It is of course realised that with the passage of time some of the satisfactory results may break down This can be expected because a biliary tract disorder and particularly a biliary dyskinesia must not be regarded as an isolated incident in the patient s life but as the disorder of a life time It also seems reasonable to assume that using the methods

I have outlined it is possible not only to offer an 80% chance of cure to the patients who still complain of symptoms after a cholecystectomy but to a large extent prevent the persistence or recurrence of those symptoms following a cholecystectomy

CONCLUSIONS

Biliary dyskinesia is a common abnormality being present in two thirds of patients suffering from biliary tract disorders It is the cause of symptoms in those patients who though presenting typical biliary symptoms have a normal classical cholecysto gram

Biliary dyskinesia is one of the main causes of the persistence or recurrence of symptoms after cholecystectomy and its recogni tion and treatment at the primary operation will go a long way *to prevent the presistence or recurrence of symptoms after the* removal of the gallbladder It may be treated surgically with a considerable degree of success both as a primary condition and in the Post cholecystectomy syndrome

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POSTCHOLECYSTECTOMY SYNDROME

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THE term postcholecystectomy syndrome implies that this entity is surgically created. Additional factors of importance in this syndrome, however, include judgment, diagnostic accuracy, technical ability and knowledge of surgical anatomy. Definitive properly performed operation with restoration of disturbed circulation and excretion of bile unquestionably achieves well being in many patients chronically disabled by disease of the biliary tract. Improper or ill advised operative intervention, however, frequently results in profound and protracted morbidity and in *some instances chronic debility. The term postcholecystectomy* syndrome, therefore, in its composite pathogenesis carries an indictment for internist and surgeon alike. Even when both have ably performed their assignments, creation or persistence of a group of ill defined manifestations that characterize this syndrome may nullify a justified procedure because of pre-existent associated malfunctions not amenable to biliary surgery, unavoidable physiologic and mechanical disturbances associated with the operation, or potential mishaps inherent in any involved technical procedure. Postcholecystectomy syndrome, partially a misnomer, is, therefore, the persistence, recurrence or occurrence after cholecystectomy of usually painful dyspeptic manifestations referable to the biliary tract with or without choledochal obstruction or inflammation. Berk[1] has defined the condition simply

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a term of reference to the situation in patients with symptoms after cholecystectomy

Among the descriptive diagnostic terms that have been applied to the syndrome are biliary dyskinesia [2] biliary dyssynergia cystic duct remnant [3] cystic duct stump [4] reformed gallbladder [3,6] recurrent biliary tract syndrome amputation neuroma traumatic neuroma [7] residual choledochal stones [8] residual hepatitis cholangitis postoperative bile duct stricture [9] stenosis of the sphincter of Oddi [10] and pancreatitis

Intravenous cholangiography enhanced by opiate induced spasm and cholecystokinetic relaxation of the sphincter of Oddi has greatly advanced our understanding of the enumerated occurences and often permits classification by pathogenesis rather than by the encompassing term postcholecystectomy syndrome

The term therefore encompasses a number of entities a variety of etiologic factors and divergent pathophysiologic changes that require meticulous diagnostic evaluation and intricate ingenious surgical correction supported by intelligent analytic and medical management Division of these entities in relation to their more characteristic types therefore seems desirable (Table I)

TABLE I

TYPES OF POSTCHOLECYSTECTOMY SYNDROMES

Type I *Persistence of precholecystectomy manifestations*

A Diagnostic errors with improper implication of the gallbladder for manifestations resulting from concomitant disease or for functional complaints

B Surgical failure to relieve choledochal obstructive manifestations pain jaundice cholangitis

Type II *Recurrence of precholecystectomy manifestations* Early return of obstructive pain jaundice or cholangitis most often results from surgical failure to relieve completely the source of choledochal obstruction

Type III *True postcholecystectomy syndrome*

A Delayed recurrence of precholecystectomy manifestations related to choledochal obstruction

1. Cholangitis
2. Formation of stones
3. Choledochitis
4. Pancreatitis

B Development of postprandial complaints related to faulty digestion of fatty foods upper abdominal discomfort pain with or without nausea and vomiting

C Biliary dyskinesia or dyssynergia

D Surgical errors
1. Cystic duct remnant
2. Gallbladder remnant
3. Stenosing choledochitis
4. Traumatic lesions formation of fistula (internal and external) choledochal section or ligation

E Pancreatitis (traumatic)

F Biliary cirrhosis

G Carcinoma of
1. Pancreas
2. Ampulla of Vater
3. Common duct

H Pericholedochal and periantroduodenal adhesions

I Traumatic neuroma

A series of 147 cases gathered from three sources (Browne McHardy Clinic Touro Infirmary and Charity Hospital New Orleans Louisiana) *during a period of twenty years (1937 1957)* and classified as postcholecystectomy syndrome includes cases from general practitioners general surgeons university teaching service private and public wards The picture is therefore composite requires analysis in several categories in addition to classification of type (Table II) and permits limited statistical conclusions Seventy nine patients were reoperated on and the diagnosis was relatively definitive the 68 not subjected to additional operation may include some instances of diagnostic inconclusiveness The composite picture does not permit an estimate of the incidence of complications

On the gastrointestinal service however when patients were seen before operation and were available for re examinaton thereafter during the same period the incidence of this complication based on readmission to the hospital was 7 5 per cent (39 among 520 cholecystectomies) Reoperation was necessary in 5 per cent (26 patients) Obviously patients whose complications were not severe enough to require rehospitalization were lost to such evaluation attenuating the accuracy of the estimate somewhat This figure is considerably lower than that obtained by Sheila Sherlock (17 to 33 per cent)

TABLE II

DISTRIBUTION OF 147 CASES OF POSTCHOLECYSTECTOMY SYNDROME

		Cases	*%*	*% of Total*
Type I	Persistence of precholecystectomy manifestations			
	Diagnostic error	43	57	
	Associated biliary disease	20	27	
	Surgical failure	12	16	
	Total	75	100	51%
Type II	Early recurrence of precholecystectomy manifestations			
	Diagnostic error	9	31	
	Associated biliary disease	12	41	
	Surgical failure	8	28	
	Total	29	100	20%
Type III	True postcholecystectomy syndrome			
	Diagnostic error	4	9	
	Associated biliary disease	9	21	
	Surgical failure	30	70	
	Total	43	100	29%

CAUSAL ANALYSIS

A Diagnostic Error (40 per cent of 147 cases)

When doubt renders exploratory laparotomy essential to a definitive diagnosis it should be justified on this basis rather than on the vague suspicion of gallbladder disease

More than a third of the 147 cases in this series resulted from erroneous diagnostic analysis either there was no significant cholecystic disease or the existing gallbladder abnormality was not responsible for the entire clinical picture for which cholesys tectomy was performed It is of interest and importance that into this category fell the largest group of persistent precholecystec tomy manifestations but the least of those classified as true post cholecystectomy syndrome

In the Type I category (persistent manifestations) were pri marily *those patients who had functional dyspeptic* complaints Twenty four had previous surgical experience (appendectomy) for the same symptoms 13 of these and 17 others were found to be entirely free of organic disease Fourteen of the group how ever had significant organic disease outside the biliary tract that may have explained their symptoms peptic ulcer in 5 esophageal hiatal hernia in 3 gastric carcinoma in 1 arthritis of the dorsal spine in 2 coronary heart disease in 2 esophageal achalasia in 1

Early recurrent symptoms occurred in 9 patients as *the result of* diagnostic error Only 4 had no organic disease In 2 patients the esophagitis of hiatal hernia remained quiescent for several weeks postoperatively and apparently the rest period produced tempo rary relief in 2 patients with duodenal ulcer and in 1 with chan nel ulcer All 3 later experienced complications that required definitive operation

True cholecystectomy syndrome in the form of biliary dyski nesia occurred in 5 patients who had normally functioning *non* calculous gallbladders removed As far as can be determined no preoperative organic disease had existed

Despite thorough careful preoperative diagnostic survey a certain number of patients will undergo operation with a pre sumptive diagnosis of cholecystitis with or without cholelithiasis The question arises as to whether the nonoffending gallbladder

should be removed to justify the diagnostic error Apparently patients with ulcer do poorly after cholecystectomy Removal of a functioning gallbladder may often precipitate mechanistic disturbances simulating dyskinesia [11]

B Associated Biliary Disease (28 per cent of 147 cases)

Incomplete diagnosis to some degree may be classified as a diagnostic error These patients were grouped with those with associated disease in that while acute or chronic cholecystitis with or without cholelithiasis existed as a true surgical indication in 41 patients and symptoms related thereto were relieved disease of the biliary tract was either causal concomitant or the result of the cholecystic disease that persisted recurred or followed operation to impair surgical success We have taken the liberty of including the liver and pancreas as biliary because of their common excretory pathways There were 17 patients each with hepatic and pancreatic disturbance and 7 with choledochal difficulty The hepatic diseases histologically established included pigment or biliary cirrhosis probably the result of prolonged extrahepatic obstructive jaundice in 3 portal cirrhosis in 8 and severe hepatic fatty infiltration in 6 5 of whom had hepatic inflammatory changes

In the pancreatic category 7 patients had acute pancreatic edema (3 with jaundice) associated with acute cholecystitis Four were classified as recurrent pancreatitis with mild steatorrhea associated with symptomatic cholelithiasis Two of 4 patients with definite calcareous pancreatitis had manifestations of pain alone 1 had pain with diabetes and 1 pain with steatorrhea In 2 patients perforation of an ulcer into the pancreas explained recurrent hyperbilirubinemic pain Choledochal difficulty was the associated biliary disease in 7 patients 5 of whom had inflammatory choledochitis and 2 of whom had fibrosis and stricture of the terminal segment of the common duct

Persistence of symptoms represented almost half the cases in this category (20 patients) Biliary cirrhosis with jaundice in 2 patients portal cirrhosis with impaired bromsulfalein excretion in 6 and fatty infiltration seen at biopsy in 3 persisted after re

moval of a calculous gallbladder On re examination later however the jaundice was seen to have cleared gradually in 1 patient with biliary cirrhosis and the fatty changes were noted to have subsided These changes were confirmed by biopsy

Pancreatitis as an acute edematous phase after removal of an acute gallbladder persisted in 3 patients in the postoperative period for an average of eight weeks before gradual subsidence The 4 patients with calcareous pancreatitis were not benefited by cholecystectomy

Early recurrence after initial histologic clearance of fatty changes seen at hepatic biopsy occurred in 2 patients with preoperative hepatic tenderness and anorexia Pancreatitis with pain and steatorrhea recurred despite removal of a calculous gallbladder In 4 patients acute edematous pancreatitis at cholecystectomy recurred after operation This is in sharp contrast with the report of complete recovery of all instances of acute pancreatitis associated with acute cholecystitis [1] Hyperbilirubinemia from perforation of an ulcer into the pancreas in 2 patients improved for a period after cholecystectomy but recurred and required more definitive operation

When associated disease of the biliary tract exists in patients who undergo cholecystectomy for cholecystic disease the operation does not usually alter the biliary disease

C Surgical Failure (34 per cent of 147 cases)

Surgical failure contributed 70 per cent of the cases characterized as true postcholecystectomy syndromes From this figure is derived the term for this composite clinical entity in most of these cases Operation however was justified in all instances and a reasonable explanation existed for the occurrence

Altogether 50 cases resulted from incomplete or unsuccessful operation residual choledochal calculi in 12 palliative cholecystostomies in 4 cystic duct remnant in 9 and gallbladder remnant in 4 Fibrosis or stricture of the terminal choledochus or sphincter of Oddi in 5 cases chronic pancreatitis with partial choledochal compression in 3 choledochal malignant disease in 1 and pancreatic carcinoma in 4 would likely be considered

surgical oversights One case each of stenosing choledochitis traumatic neuroma traumatic pancreatitis and periantroduodenal adhesions and 2 each of pericholedochal adhesions and formation of fistula comprise a pardonable balance

Adhesions Besides the factors already considered rarer occurrences of pericholedochal and periduodenal adhesions may create respectively choledochal angulation obstruction and duodenal obstruction or ileus Although these entities are probably unusual and not established contributors of postcholecystectomy syndrome 2 fairly conclusive instances are included in our series

Physiologic derangements wherein the digestive system must adjust to loss of bile reservoir to hormonal (cholecystokinin) stimulation which apparently normally activates the reciprocal mechanism of cholecystic contraction and relaxation of the sphincter of Oddi are demonstrable in a morphine reproducible sphincteric spasm or digestive disturbances which persist for a variable postoperative period These disturbances appear to be minimal and brief when a chronically nonfunctioning gallbladder is removed more severe and more protracted when the acute nonfunctioning or functioning gallbladder is removed Dyskinesic or pain of incoordinating ductal motility *per se* has rarely been encountered in our patients in whom a nonfunctioning gallbladder of long duration was removed To functional derangement alone Sherlock applies the term postcholecystectomy syndrome [13]

Choledochostomy Drainage by choledochostomy regardless of the length of the T tube limbs is frequently complicated by regurgitation of duodenal content with peptic activity into the common duct The importance of this observation in the course of our recent study of choledochal bile is as yet undetermined but the probable relation to choledochitis and formation of stricture is hypothesized

TREATMENT

The management of postcholecystectomy states demands determination of the cause in each case and tailoring of therapy accordingly (Table III) Obviously patients with surgically

TABLE III

CAUSE TYPE AND TREATMENT OF 147 CASES OF POSTCHOLECYSTECTOMY SYNDROME

Cause	*No*	%
Diagnostic error	56	38
Associated biliary disease	41	28
Surgical failure	50	34
	147	100
Final Diagnosis		
Nonbiliary		
Functional	30	67
Organic	14	33
	44	100
Biliary		
Physiologic	33	32
Mechanical	70	68
	103	100
Management		
Re operation	79	53
Medical	68	47
	147	100

correctable mechanical difficulties either biliary or extrabiliary should be operated on again after careful diagnostic judgment and preparation In many such instances the patient is a poor operative risk whose physical status further declines with undue procrastination

The medical issues encompass the management of nonbiliary organic illness the problems of psychosomatic direction of the functional disturbances and the control of disturbed biliary secretion and function This discussion is restricted to those patients who after recovery from biliary operation are dis

charged to the medical service with or without choledochostomy drains and free of mechanical or associated nonbiliary symptomatic disease These patients who have been dyspeptics by virtue of a malfunctioning gallbladder a ductal system subjected to varying degrees of obstruction and associated inflammatory or damaged biliary structures (liver or pancreas) are too often discharged on a "low fat diet" by the mechanically minded physician who considers simple excision of a diseased organ the complete answer to the problem

The dietary program should be individualized to hepatic ductal cholesterol and pancreatic status of the patient In most instances it will be a high carbohydrate moderate protein restricted fat (cooked) regimen Obesity should be corrected Regularity of eating and avoidance of between meal feedings are essential to re establishment of dietary desirable biliary flow

Induced hydrocholeresis by use of dehydrocholic acid (Decholin®) or florantyrone (Zanchol®) is of established value in increasing the volume of biliary flow through a recovering ductal system In choledocostomized patients during the recovery period when bile has dropped remarkably in volume and has become concentrated and when signs suggestive of choledochitis have developed symptomatic and physiologic response to increased biliary flow have followed their administration Decholin® has the advantage of intravenous innocuousness when parenteral administration is imperative

Cholecystokinetic effect inducing relaxation of the sphincter of Oddi has been satisfactorily achieved in the patient with morphine Cholografin® demonstrated "Odditis" by the use of D Glucitol (ProBilagol®) an agent which simulates olive oil magnesium sulfate and the fatty meal in inducing cholecystokinetic gallbladder emptying during cholecystography This agent additionally may enhance B 12 absorption [14]

Bile salts and acids should also be administered when absorption of fat is impaired

Avoidance of opiates that might precipitate dyskinesia and use of nitrites in the presence of dssynergia are imperative We have not been able to discover an antispasmodic action for any of the

atropine like drugs in relieving induced choledochal pressure

Beyond these measures there is the need for the patient to understand the overall requirements of adjusted habits and living to the degree of existing and persisting impairment of the biliary phase of digestion

DISCUSSION

When it is appreciated by experience that biliary pain does not conform to any set pattern in the great majority of cases there becomes greater tolerance for the high incidence of diagnostic error Characteristic biliary colic with back radiation nausea vomiting and localized biliary tenderness do not require unusual diagnostic acuity

Most patients with gallbladder disease complain of a variable degree of food intolerance postprandial distention eructation pyrosis gas flatulence substernal oppression nausea and vomiting This group of nonspecific symptoms may be elicited from most functional dyspeptics are not characteristic of gallbladder disease should not be considered diagnostic and relief from them by cholecystectomy should not be anticipated

The composite diagnosis of gallbladder disease requires conservatism and judgment[1] in evaluating the patient for cholecystectomy In such discussion it should take precedence over the treatment applicable surgical or medical to circumstances present after recovery from removal of the gallbladder Definitive diagnosis should preclude over enthusiastic surgical prediction for therein shall be recognized contributing factors other than the gallbladder that excite digestive discomfort Saints Triad cholecystitis esophageal hiatal hernia and colonic diverticulosis so common to the elderly should never be forgotten The frequent concomitancy with gallbladder disease of peptic ulcer and coronary heart disease in addition to those component diseases of the biliary tract pancreatopathies and hepatopathies often require the diagnosis of cholelithiasis to be modified in relation to associated diseases

As the operative technique of simple cholecystectomy must now be fairly standardized throughout the world it follows that

the discrepancy in results obtained must find its explanation largely in differing case selection" concludes Goldsmith in a discussion of the relative infrequency of postcholecystectomy syndrome in Britain as compared with elsewhere [15] While the technique may be standardized surgeons are not nor are circumstances under which cholecystectomy may be performed Avoidance of surgery in acute cholecystitis when feasible should be a primary premise The masking of normal and abnormal anatomic relations by inflammatory reaction and the increased liability to common duct injury under such circumstances should be recognized as a prominent cause of surgical failure [17] Since the increasing incidence of acute cholecystitis and of carcinoma of the gallbladder [9] in the aged has been presented as indication for cholecystectomy in the asymptomatic calculous gallbladder in our population component of most rapidly increasing percentage we must be alert to the potentiality of an increasing incidence of postcholecystectomy difficulty in bad risk patients if we are not comprehensive in our diagnostic evaluation

In evaluation too many patients (approximately 40 per cent) describe their status as "no better or worse" in respect to cholecystectomy done for noncalculous cholecystitis or non-colic producing calculous cholecystic disease Fortunately most patients suffering from acute cholecystitis or biliary colic related to cholelithiasis (approximately 85 per cent) are relieved by cholecystectomy It therefore appears that the degree of speculation in performing cholecystectomy for chronic noncalculous cholecystitis is too great to permit its election while the assessment of benefit in acute cholecystitis and biliary colic justifies the risk of postoperative difficulty

The source of pain in the postcholecystectomy patient who has no residual organic disease is not satisfactorily answered The choledochus has been found to be enlarged beyond a diameter of 6 mm in most such patients [21] This enlargement has been theorized to result from increased pressure in the biliary tree
but from residual obstructive disease If however the theory of cholecystokinetic action is applicable to the postcholecystectomy occurrence of dyskinesic pain and such is easily rationalized

when pain reducible by opiates and relieved when hormonal stimulation is excited by duodenal application of olive oil magnesium sulfate or ProBilagol® there is not justification for reoperation without more careful medical management

SUMMARY

1 A survey of 147 patients with postcholecystectomy difficulty is analyzed

2 The term postcholecystectomy syndrome is too inclusive and too often misinterpreted Nomenclature for each pathophysiological mechanism should be established

3 The incidence of postcholecystectomy difficulty is too frequent and too severe in significance to permit injudicious and unskilled surgery on the biliary tract

4 Good medical analysis should prevent unnecessary surgery

5 Instances of physiologic derangement after cholecystectomy are in many instances amenable to medical management

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THE MALABSORPTION SYNDROME

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INTRODUCTION

THE malabsorption syndrome may be defined as a group of related symptoms which develop when the usual constituents of the diet including vitamins minerals and even water are not absorbed in a normal fashion In his recent monograph on the malabsorption syndrome [1] Adlersberg speaks of the primary malabsorption syndrome in which there are no clinical roentgenologic or post mortem evidences of gross organic disease entities involving the gastrointestinal tract pancreas or liver and secondary malabsorption syndromes in which gross pathologic alterations may be encountered in the gastrointestinal tract or after effects of surgical procedures pathologic conditions in the pancreas or changes in the liver or biliary tree

In classifying the malabsorption syndrome it would seem reasonable to take into consideration its fundamental causes In general when the malabsorption syndrome develops either digestion is impaired and absorption is normal or absorption is impaired and digestion is normal Since intelligent treatment of the syndrome is dependent upon which defect is present such a classification has clinical and practical usefulness

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CLASSIFICATION

A convenient working classification of the more important conditions resulting in malabsorption is as follows

I Digestion impaired—Absorption normal
- A Disease of the pancreas
  1. Chronic relapsing pancreatitis
  2. Carcinoma
  3. Cystic fibrosis
- B Diseases of the liver or biliary tract
  1. Advanced liver disease
  2. Common duct obstruction
- C Following surgical procedures
  1. Gastric resection
  2. Gastroenterostomy
  3. Gastroileostomy

II Absorption impaired—Digestion normal
- A Diseases of the small intestine
  1. Sprue
     - a Tropical
     - b Non tropical
     - c Celiac disease
  2. Regional enteritis
  3. Whipple s disease
  4. Lymphoma
  5. Tuberculosis of mesenteric glands
  6. Amyloidosis
  7. Scleroderma
- B Resection of 50% or more of small intestine
- C Radiation injury to the small intestine

CLINICAL PICTURE

The underlying disease which results in the malabsorption syndrome often presents a characteristic picture and the diagnosis may be made by history and physical examination alone However the malabsorption syndrome itself is essentially the same regardless of the underlying cause The clinical picture of this syndrome necessarily will vary according to the degree of mal absorption Thus in patients having only slight impairment of absorption there may be no symptoms whatever and the con dition is discovered only by appropriate laboratory studies

whereas in advanced malabsorption the diagnosis is readily apparent The most constant symptoms are weight loss at times in spite of a good appetite and apparent adequate ingestion of food weakness fatigability and diarrhea The diarrhea with or without gross steatorrhea will vary in severity and is frequently nocturnal Macrocytic anemia is to be expected in sprue and following total gastrectomy and iron deficiency anemias are fairly common in the malabsorption syndrome regardless of cause

Less frequently one sees vitamin deficiencies especially those related to the fat soluble vitamins D and K resulting in osteomalacia and a bleeding tendency Glossitis stomatitis and peripheral neuritis used to be common but with the widespread use of B complex vitamins these are rarely seen today Dependent edema from a low serum albumin and tetany due to hypocalcemia are to be expected in the advanced case but in our experience are relatively rare

X ray findings in the malabsorption syndrome are obviously dependent upon the underlying disease Thus there may be extensive calcification in the pancreas a stone in the common duct a gastroenterostomy or gastric resection but these findings do not predicate impairment of digestion with resulting malabsorption On the contrary the demonstration of generalized disease of the small bowel invariably is associated with varying degrees of malabsorption One hastens to point out that the underlying disease of the small intestine often cannot be diagnosed by x ray alone For illustration the x ray findings in non tropical sprue may be indistinguishable from those in patients having Whipple s disease In pancreatitis on the contrary the small bowel pattern may be entirely normal

As pointed out earlier the malabsorption syndrome is a rather loose term applied to a group of related symptoms resulting from a variety of causes Obviously in the malabsorption state any or all of the ingredients of the diet may be poorly absorbed but if there is any impairment of absorption fat and fat soluble substances are likely to be affected While it is realized that malab-

sorption and steatorrhea are not synonymous for practical purposes the terms may be used interchangeably

STEATORRHEA

Steatorrhea implies a diarrhea characterized by the passage of soft or watery pale frothy greasy voluminous foul smelling stools However the dictionary defines steatorrhea as the presence of an excess of fat in the stool By this definition the passage of stools containing more fat than is found normally but not having the physical properties described above would be classified as steatorrhea Therefore the term steatorrhea should include not only frank steatorrhea with the characteristic stool but also what may be called occult steatorrhea in which an abnormal amount of fat is present although not readily apparent Actually in our experience occult steatorrhea is far more common than frank steatorrhea It would be an error therefore to assume that an excessive amount of fat in the stool necessarily produces diarrhea or if actually present that this diarrhea is steatorrhea in the sense that it is generally thought of For this reason impairment of fat absorption is not suspected in many patients merely because diarrhea is not present or the stool does not have the gross appearance usually associated with frank steatorrhea

METHODS OF DEMONSTRATION OF STEATORRHEA

1 *Inspection* When steatorrhea is marked inspection of the stool is all that is necessary to detect its presence Unfortunately in many if not in most cases an abnormal amount of fat in the stool cannot be determined by inspection alone

2 *Microscopic Examination* This method is quite simple consisting of staining the fat in the stool with a suitable reagent such as Sudan III However this stains only neutral fat and fatty acids in globule form Fatty acid crystals and soaps do not stain Therefore unless the stool *is acidified and heated to convert the* soaps to globules the demonstration of fat frequently is missed Since there is little fat in the stool of the normal individual the presence of an appreciable amount of stained globules is con

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OTHER METHODS OF DEMONSTRATING MALABSORPTION

For years the oral glucose tolerance test has been accepted as a satisfactory method of studying intestinal absorption a flat curve indicating disease of the small bowel However the validity of this test has been questioned since a flat curve may be present in normal individuals[5,6]

Recently the value of the d xylose tolerance test as a measure of intestinal absorption has been emphasized Urinary excretion following ingestion of a test meal shows a clear cut distinction between normal individuals and patients having the malabsorption syndrome secondary to disease of the small intestine provided renal function is adequate It would certainly appear that this is a reliable test within the reach of most laboratories

The vitamin A tolerance test has likewise been employed as a measure of intestinal absorption and good correlation has been demonstrated between the blood levels of vitamin A and the degree of steatorrhea as revealed by fat balance studies[8] The test however is difficult to perform and usually not practical except in a research laboratory

The chylomicron count[9] and serum turbidity[10] have been advocated as measures of fat absorption These tests however have not been widely used Serum carotene[11] recently has been proposed as a screening procedure and as such probably is worthwhile

The use of Co^{60} B_{12} has been employed as a measure of malabsorption Patients with sprue extensive regional enteritis and the blind loop syndrome will usually show impairment of absorption of B_{12} which is not correctable by the oral administration of a potent intrinsic factor[12] In the absence of pernicious anemia a positive Schilling test may be taken as evidence of malabsorption but, of course a negative test does not exclude the presence of steatorrhea

The folic acid excretion test as a measure of malabsorption was introduced in 1953[13] A recent study confirmed the validity of this test and further showed that folic acid is probably absorbed in the proximal and B_{12} in the distal small bowel[14] The technique of the test is complicated rendering it of little value outside

cusive evidence of steatorrhea provided that mineral oil which also stains in the same fashion can be excluded At best this method permits a rough estimate of the degree of steatorrhea and is of limited usefulness

3 ***Fat Balance Study*** A far more reliable method and one conventionally employed is the fat balance study However chemical determination of fecal fat is time consuming and laborious requiring a metabolic ward and from five to six days or even longer for completion of the test An excess of 5 gm of fat in the stool per day is considered abnormal when on a daily intake of 50 100 gm of fat

4 ***Radioactive Tagged Lipids*** In recent years the availability of radioactive tagged lipids has offered a new approach to the problem Using a test meal containing I^{131} tagged triolein characteristic and reproducible curves representing blood levels of radioactivity may be expected in the normal individual and less than 5% of the radioactive content of the test meal is recoverable in the 48 to 72 hour collection of the stool [4]

In frank steatorrhea regardless of cause blood levels of I^{131} are depressed and the radioactive content of the stool is elevated Although this inverse relationship between the blood and fecal levels of radioactivity is present in most instances of occult steatorrhea some patients with slight to moderate elevations of fecal radioactivity will have low normal or even normal blood values Therefore the radioactive content of the stool would appear to be a more sensitive and reliable index of steatorrhea than are the blood levels In many institutions great difficulty may be experienced in collecting total 48 to 72 hour stool specimens which must be free of urinary contamination On the contrary collection and analysis of blood samples at the 4th 5th and 6th hours after ingestion of the test meal is relatively simple and usually furnishes valuable information concerning the presence or absence of malabsorption within a matter of hours after beginning the test In our opinion both blood and stool determinations should be made in every case at least until their relative usefulness has been established in each laboratory

vitamin deficiencies are common and supplemental vitamin therapy is definitely indicated with special emphasis upon vitamins D and K Iron and calcium given either orally or parenterally may be required in certain patients and other hemopoietic factors B_{12} and folic acid are advisable in patients having a macrocytic anemia Many patients with diarrhea will develop a potassium deficit Therefore serum potassium should be followed closely and potassium administered as needed

TREATMENT DIGESTION IMPAIRED—ABSORPTION NORMAL

Although the above general principles of treatment are applicable to all patients with malabsorption it should be pointed out that the malabsorption syndrome is a group of related symptoms and not a disease To treat it without due regard for the underlying disorder is likely to yield discouraging results Therefore when the syndrome is encountered it is imperative that a correct diagnosis be made before initiating therapy

1 *Chronic Relapsing Pancreatitis* In patients who have had the disease over a long period of time the pancreas is gradually destroyed and pancreatic insufficiency results Dietary treatment in these cases has proved disappointing Restriction of fat will decrease the steatorrhea to some extent but a more successful approach would be an effort to correct the digestive deficiency Replacement therapy in the form of pancreatic enzymes is indicated Viokase[*] in doses of 8 12 gm per day has been tried with encouraging results A significant increase in absorption has been noted along with clinical improvement The effect of replacement therapy in a patient having a total pancreatectomy for chronic relapsing pancreatitis is shown in figure 1 Although he was never able to regain his normal weight or strength by taking pancreatic extract the patient was able to control his diarrhea and work part time When this was omitted he was completely incapacitated He died of perforation of the small bowel of undetermined cause

[*] Supplied by the Viobin Corporation Monticello Illinois

a research laboratory Preliminary reports of the use of radioactive iron in patients with steatorrhea suggest that it may likewise be useful in the study of malabsorption secondary to small bowel dysfunction [15]

DISTINCTION BETWEEN DIGESTIVE AND ABSORPTIVE MALFUNCTION

As stated previously the malabsorption syndrome may result from either an error of digestion or a defect of absorption Since the fundamental approach to therapy is dependent upon the recognition of which of these two conditions is present it becomes a matter of practical importance to make this distinction

In patients in whom the presence of steatorrhea has already been established a number of tests may be employed for this differentiation It has been shown that the absorption of d xylose is markedly impaired in patients having steatorrhea as a result of extensive small bowel disease whereas the test is normal in patients with pancreatic insufficiency Theoretically, the same results are to be expected following the use of vitamin B_{12} iron and folic acid but further work must be done before the usefulness of these procedures can be determined

By the employment of I^{131} tagged triolein followed by I^{131} tagged oleic acid in the same patient one may distinguish between a digestive and an absorptive defect When absorption is impaired both blood curves will be flat and the radioactive content of the stools will be elevated If the error is one of digestion only the triolein curve will be flat and there will be a corresponding elevation of fecal fat whereas the blood and fecal values of oleic acid will be relatively normal [16]

TREATMENT GENERAL PRINCIPLES

Since weight loss is universally present in patients having the malabsorption syndrome every effort should be made to increase their daily caloric intake The diet should be high in proteins with carbohydrates and fats as tolerated Thus a standard diet to be prescribed for all is unwise as the fat and carbohydrate content should be varied to suit the individual patient Multiple

Replacement therapy however using both pancreatic enzymes and bile salts has been disappointing in our experience Other forms of treatment including the gluten free diet and steroids have likewise failed to affect absorption significantly or result in clinical improvement in these patients

Administration of Nilevar® and anabolic agent will usually result in weight gain in normal individuals This has been tried in a small number of post gastric resection cases over a short period of time with encouraging results as illustrated by the case report shown in figure 2 It is generally accepted that patients

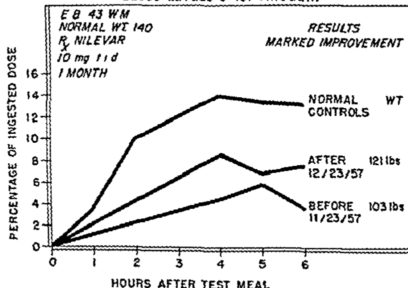


Fig 2

having a total gastrectomy will eventually develop a macrocytic anemia The effect of B_{12} upon the anemia absorption and clinical course of such a patient is shown in figure 3 No definite conclusions as to the value of these two substances used in this

Supplied by G D Searle & Co Chicago Illinois

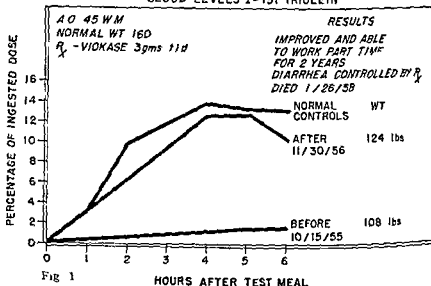


Fig 1

2 ***Malabsorption Following Surgical Procedures*** Approximately 50% of all patients who have had a subtotal resection (Billroth II) or gastroenterostomy with or without vagotomy, will have a significant loss of weight and fail to regain their normal or ideal weight While it is realized that an inadequate dietary intake is an important factor it is equally true that 50% of these patients will have impaired intestinal absorption Using I^{131} tagged lipids it was found that triolein was poorly absorbed but the absorption of oleic acid was normal in most cases [17] This tends to confirm the belief that the steatorrhea that develops in this group of patients is primarily a defect of digestion rather than an error of absorption The work of Lundh adds additional support to this hypothesis [18] He has shown that although the total secretion of the pancreas and concentration of bile after a test meal in the post resection patient were normal over a period of several hours the initial secretion was significantly diminished and adequate mixing of the test meal with digestive juices and bile was not observed

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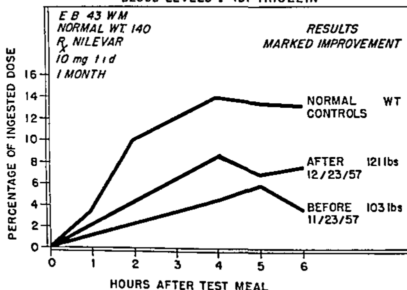


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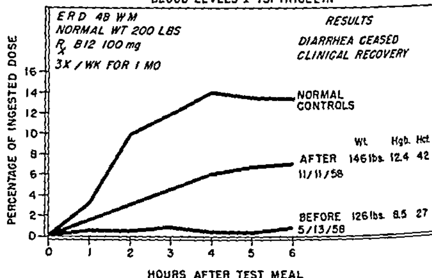


Fig 3

group of patients are justified at the present time and yet the results furnish food for thought

TREATMENT ABSORPTION IMPAIRED—DIGESTION NORMAL

1 *Sprue* At one time it was generally agreed that there was no distinction between tropical and non tropical sprue[14] However recent studies have shown that they may differ in at least one important respect namely in their response to therapy[6]

The treatment of choice in non tropical sprue is the gluten free diet[1] Although most patients respond promptly within a matter of a few days or weeks the diet should be continued for *at least six months before discarding it It is probable* that failure to improve following this form of therapy means either lack of strict adherence to the diet or a mistaken diagnosis Macrocytic anemia with associated malabsorption of Co^{60} labeled vitamin B_{12} uncorrected by the administration of intrinsic factor occurs fairly commonly in non tropical sprue Nevertheless in our experience it has been unnecessary to supplement dietary treat

ment with folic acid B_1 liver extract or minerals Six patients have been following this diet from one to five years with a complete and sustained clinical hematological and radiological remission Furthermore results of their absorption tests using the I^{131} tagged lipids have reverted partially or completely to normal Microscopic sections of the mucosa of the small intestine in patients in relapse, obtained by the intestinal biopsy tube have shown decreased numbers of flattened clubbed and atrophic villi [3] The effect of the gluten free diet upon absorption and the clinical course of a patient having sprue is shown in figure 4

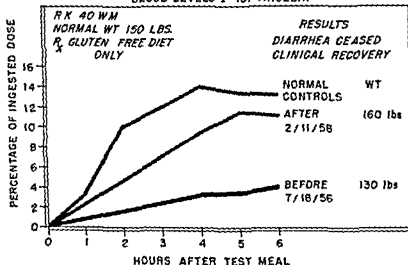


Fig 4

Recent studies would indicate that patients with tropical sprue do not respond to the gluten free diet but usually will recover after the use of folic acid liver extract or B_1 [4] Other observers have found that antibiotics are beneficial [6] The intestinal mucosa shows essentially the same changes as noted in non tropical sprue and just why there should be a difference in response to therapy is not clear

2 *Whipple's Disease* This interesting disease probably is more common than is generally appreciated There have been ten known cases at Duke Hospital within the past 22 years and doubtless there are many more than the reported 100 or more cases in the world's literature At one time the prognosis was considered hopeless and little was done other than to institute general supportive measures We now have three patients who are alive and well 30 to 52 months after the diagnosis was made On reviewing the therapy of these ten patients it is observed that the only form of treatment that was common to the survivors was antibiotics Such an observation proves nothing of course but warrants further investigation We should take the position that Whipple's disease is not necessarily fatal and that if the patient can be tided over a critical period of malnutrition recovery may take place

3 *Regional Enteritis* Recent studies would indicate that normally the majority of fat is absorbed in the upper portion of

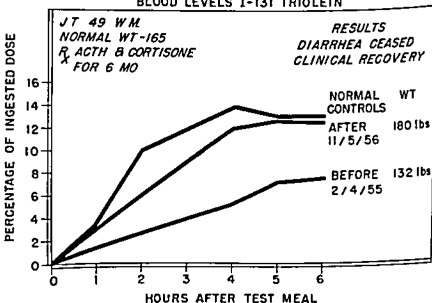


Fig 5

the small intestine Therefore the malabsorption syndrome may not develop if only the terminal ileum is involved When present we have found steroids distinctly beneficial with the absorption of I^{131} tagged lipids returning to normal along with clinical improvement The effect of steroids upon the absorption and clinical course of a patient having regional enteritis is shown in figure 5

SUMMARY

While the full blown malabsorption syndrome which develops in sprue and celiac disease is relatively rare in this country it would appear that varying degrees of malabsorption following partial gastric resection and in diseases of the liver pancreas and small intestine are common and frequently overlooked The distinction between malabsorption resulting from a defect of digestion and from an error of absorption is important and can be made readily by the use of I^{131} tagged lipids The institution of proper treatment after the correct diagnosis has been made is gratifying in many cases

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PATHOPHYSIOLOGY AND TREATMENT OF INFECTIOUS DIARRHEAS

HENRY D BRAINERD M D

THE infectious diarrheas are among our most common illnesses and by and large are more important by reason of their frequency than because of their seriousness although there are notable exceptions to this statement

I think it might be interesting to review what relatively little we know of the causation of this problem and to discuss the treatment where we have specific measures

You are all aware of the many patterns of so called acute gastroenteritis that appear year after year and sweep through the population causing them considerable unhappiness There are rarely any serious complications except perhaps in a few old or debilitated people Our knowledge of what causes this syndrome is surprisingly sparse when we think how common it is Furthermore it certainly represents a fertile field for study now that we have newer techniques for isolation of viruses Most of the acute diarrheas are presumably of viral origin and it is likely that there are at least a handful of such viruses a few of which have been tentatively sifted out of this group Unfortunately in no instance has there been isolation and cultivation of a virus which would be definitive but rather information has been gained by passage of *infective material to human volunteers and study of the incubation period* and clinical characteristics of the disease

William Watt Kerr Professor of Medicine University of California School of Medicine San Francisco

9 FRAZER A C and STEWART H C Ultramicroscopic particles in normal human blood *J Physiol* 90 18 1937

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characteristic of a respiratory mode of spread in contrast to the ingestion mode These types of gastroenteritis three in all are shortlived and benign

There is another probable entity—epidemic diarrhea of the new born of viral etiology and this is much less benign This disease as you are aware affects primarily newborn infants and tends to be very severe and persistent as well as a cause of high mortality in newborns The mortality even in the best circumstances is approximately 10 per cent This type also affects adults in an epidemic which was encountered about ten years ago the entire ward staff became ill with a rather vicious type of gastroenteritis which was febrile and persisted for approximately a week and differed quite sharply from the more common pattern A pre sumed viral agent[4] has been isolated from at least one type of diarrhea of the newborn which produces a peculiar lesion of the rabbit s cornea which resembles remotely the lesion produced by herpes simplex virus although apparently there is no relation There is as I implied some debate about the validity of this observation A similar agent has been transmitted to calves by Light and Hodes[6] and may well be the same pathogen So this then is another probable viral cause of diarrhea which differs from the others in being very much more severe even in adults This represents the sum total of our knowledge small as it is concerning the viral diarrheas There is however one point I would like to make clear and that is the matter of influenza or intestinal influenza with numerous variations There is actually no such thing Influenza virus characteristically produces few or no gastrointestinal symptoms which are at the most usually limited to nausea and vomiting and in less than 10 per cent of cases influenza produces diarrhea and those cases are usually in people in whom anything produces diarrhea We have studied numerous outbreaks of various gastroenteritis for the presence of influenza virus or have attemped to demonstrate a rise in titer of influenza antibodies and have failed The treatment of these viral diarrheas is as far as any specific approach goes completely nil There is no chemotherapeutic agent which affects the course of these dis eases in any way It is hoped that at some time it may be possible

There are probably four entities which in some way have been separated from the total group of viral diarrheas although this is not certain The first of these which represents a very common pattern is the so called Marcy type which was demonstrated by Gordon *et al*[1] in New York This is a viral agent which is present in stools of afflicted individuals and can be transmitted by ingestion of bacteria free stool filtrates Also interestingly enough it can be transmitted by ingestion of throat washings of patients by volunteers This produces a typical although not distinctive disease after an incubation period of one to five days manifested by nausea vomiting and diarrhea and which is characteristically afebrile This latter serves to distinguish this particular pattern from some of the others This type lasts two or three days and is utterly benign

A second variety which was demonstrated by Jordan has a different pattern and is characterized by fever usually not very high and by rather distressing cramps but generally by absence of diarrhea I am sure you have all seen this particular syndrome This type of gastroenteritis is more troublesome because it frequently brings up the question of an acute surgical abdomen and at times is somewhat difficult to distinguish from it although as a rule the physical findings in the abdomen are quite minimal This agent can be transmitted only by ingestion of filtered stool and not by throat washings and thus differs clinically and etiologically from the Marcy type This variety is called the FF type

Another probable agent was isolated by Reimann[3] It produces much the same picture as the Marcy agent i e nausea vomiting and diarrhea of the classic pattern This variety differs however in that it can be transmitted by inhaling throat washings This implies of course that it has a respiratory mode of spread I am sure you all have encountered epidemics where this route has seemed the most likely The epidemics presumed due to this particular viral agent follow the pattern of respiratory epidemics in that they are very sharp in outbreak A whole office force will be wiped out temporarily in a few days and yet they will all be back at work shortly This explosive pattern is

characteristic of a respiratory mode of spread in contrast to the ingestion mode These types of gastroenteritis three in all are shortlived and benign

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to develop polyvalent virus vaccine for at least several of these agents Until the viruses are actually isolated by culture or chick embryo inoculation this is impossible Treatment with any sort of antispasmodic is helpful accompanied by limitation of ingestion of food and in the occasional instance the replacement of fluid and electrolytes when necessary

In contrast to the viral group the bacterial diarrheas are considerably more formidable The classic shigellosis or bacillary dysentery may appear to be a rare disease yet in this state particularly in the Central Valley every summer a rather large number are encountered and in the isolation wards of the San Francisco Hospital it is quite common during the summer months It is most common to find it in young children but a significant number of adults with shigellosis are seen This is a severe enteritis usually quite sharply febrile and lasting untreated something approaching a week as a rule and followed in some patients by a more persistent diarrhea and a syndrome resembling at times ulcerative colitis The organism is not invasive with the rarest of exceptions This is purely an enteric infection with toxemia It is rather difficult to isolate the organism from the stool at times and one must use very careful techniques We have found the most satisfactory way to be by using a sterile enema tube to obtain rectal washings which are then cultured on an appropriate medium The treatment of shigellosis is for the most part quite satisfactory There are a variety of chemotherapeutic agents which are effective The sulfonamides either absorbable or the so called bowel sulfonamides such as Sulfasuxidine® and Sulfathalidine® are quite effective Any of the tetracycline group of drugs is likewise effective Oral streptomycin and oral neomycin are apparently also effective although perhaps in the treatment of the acute form not as advisable Very important in this group particularly in children is the management of fluid and electrolyte loss Most astonishing losses of fluid occur in infants sometimes in newborn infants half the body weight may be lost in the space of a very few hours resulting in profound shock Treatment of this is most important One should also recall the possibility if diarrhea is at all prolonged of marked hypokalemia The treat

ment of the Shigella carrier state unlike the disease is quite unsatisfactory The drug which has had the highest rate of success interestingly enough is oral polymyxin

Salmonella which is even more common in this area produces several patterns of disease that it might be well to review briefly The syndrome most under discussion today is acute Salmonella gastroenteritis usually arising from the ingestion of contaminated food A second pattern is the typhoidal type of disease and we should caution that while diarrhea is commonplace in typhoid fever it is not uniform and certainly one is not able to exclude the diagnosis of typhoid fever in the absence of diarrhea The third pattern of salmonellosis is the so called septico pyemic variety where there is persistent bacteremia and focalization in various areas This is particularly common in children but can occur in any age and results in all sorts of bizarre syndromes i e salmonella meningitis osteomyelitis pneumonia and the like and carries with it a very high mortality While any of the many varieties of Salmonella can produce any of the variants in clinical picture certain Salmonella are usually associated with a single pattern For instance the commonest cause of gastroenteritis is S enteritidis S typhi is the commonest cause of the typhoidal type and S choleraesuis is the commonest cause of the septico pyemic variety The recognition of a Salmonella gastroenteritis is not difficult although it may be impossible to distinguish it clinically from shigellosis and the diarrhea is usually quite profound

We have found one screening technique that helps us to separate with a fairly high degree of reliability acute bacterial dysentery from viral diarrheas and that is a methylene blue stained smear of the stool In the viral varieties the cell type in the stool is characteristically mononuclear whereas in bacterial diarrheas including shigellosis and salmonellosis polymorphonuclear leucocytes are usually present in abundance Blood is quite commonly present in the stools in bacterial diarrheas whereas this is quite rare in viral diseases

The ultimate diagnosis of course usually depends on the isolation of the Salmonella from the stool This is usually not particularly difficult in contrast to Shigella

The different varieties of Salmonella may be determined by elaborate techniques according to their antigenic pattern The principal value of separating them is epidemiological

The treatment of salmonellosis other than replacement of fluid and electrolytes is limited to chloramphenicol It is questionable that in the milder Salmonella gastroenteritis specific treatment is necessary However in those who are sick and certainly in those who have bacteremia I think it is There are a variety of chemotherapeutic agents which are active against this organism in vitro but the only one which is active in vivo with any degree of constancy is chloramphenicol and this is presumed to be due to the fact that the organism is so often present intracellularly and simply not accessible to any other agent except chloramphenicol which has the property of being able to penetrate the cell wall readily

Treatment in the typhoidal type should be prolonged after the usually suggested course of chloramphenicol of two weeks We have observed a rather disheartening incidence of relapse in patients stopped after two weeks and I think the course of treatment should be at least three weeks In the very severely ill patient who has salmonellosis the use of adrenal steroids may be considered and this is probably one of the few infections where there is some rationale These organisms produce many of their manifestations by means of endotoxin action The cortico steroids have been demonstrated to have the property of neutralizing the effect of endotoxins This does not apply to exotoxins which incidentally are not produced by these organisms So in patients who appear toxic the simultaneous use of specific chemotherapy and corticosteroids may well be indicated

The Salmonella carrier state which occurs unfortunately rather frequently following infections and is also found not rarely in the population at large is one of the worst chemotherapeutic problems with which we have to deal and is almost a hopeless one If a patient sheds Salmonella including S typhi following the disease and does not clear in a few weeks he is quite likely to remain a carrier for some time and perhaps permanently Choramphenicol which is quite effective in the acute disease appears to have

no effect whatsoever on the carrier state nor do any of the other standard chemotherapeutic agents We have had two patients however who have been able to clear with penicillin One does not think of penicillin as being active against gram negative organisms and indeed it is not very active but some Salmonella are inhibited by very large amounts of penicillin and fortunately penicillin can be rather easily concentrated in the gallbladder some fifty times or so By giving massive doses of penicillin we have been able to abolish the carrier state in a few gallbladder carriers This is not a particularly practical procedure but this happens once in a while and is perhaps worthwhile recalling

Perhaps the commonest bacterial diarrhea we see today is one largely of our own doing and this is staphylococcal diarrhea There are two forms of this disease which I think we should distinguish in our minds The one is staphylococcal food poisoning with which we are all familiar and undoubtedly all have had This is not an infection but is caused by a preformed enterotoxin which is a violent gastrointestinal irritant and which after a short incubation period usually four to twelve hours produces a syndrome with which you are all familiar Staphylococcal food poisoning may in severe cases produce neurological symptoms which have on many occasions caused suspicions of the possibility of botulism I refer to the weakness and blurring of vision which occur quite commonly in severe staphylococcal food poisoning but may be confused with the early cranial nerve lesions of botulism which however is rather rarely associated with a gastroenteritis of any proportion often quite the contrary The treatment of staphylococcic diarrhea consists primarily if necessary in replacement of fluid and electrolytes At times this is truly an emergency procedure These patients mav be in quite profound shock and may be very dehydrated all in the space of a very brief time We had a house officer in the San Francisco Hospital who coined a very apt term for people coming in with severe diarrhea of this variety He called them "instant people if you simply added some fluid they were re constituted This is the case with staphylococcal diarrhea It is violent but brief and except in

debilitated persons is not associated with mortality

The other type of staphylococcal diarrhea is very much more important and unfortunately is a disease of hospitals and is largely produced by doctors This is of course staphylococcal enterocolitis which has probably always existed and never been emphasized until recent years This occurs generally speaking in two circumstances in people who have been operated on and particularly whose gastrointestinal tracts have been operated on (this is by no means exclusive) and in people who have received chemotherapeutic agents most notoriously the tetracycline drugs and particularly oxytetracycline although this may simply represent the fact that this drug was used so much more frequently than other tetracyclines until recently

The disease arises by reason of change in bowel flora There seems necessarily to be some sort of balance in the flora of our respiratory and gastrointestinal tract If this be altered unhappy events may transpire and result in super infections with a staphylococcus resistant to the drug being administered in a debilitated person This not only may produce the most violent of enterocolitis but also is not rarely associated with bacteremia and sometimes with diseases such as lung abscess meningitis or the like I think prevention here is the watch word and I am sure now in most hospital routines so called chemoprophylaxis is decreasing and particularly the routine use of tetracycline drugs following one sort of surgery or another I think in any instance where we are thinking about chemoprophylaxis in any disease *we might weigh very carefully the risk of drug administration* against the risk of the infection we are anticipating

Staphylococcal enterocolitis must be suspected in any one having a diarrhea arising following surgery or most particularly when associated with chemotherapy particularly with tetracycline However this causes at times unnecessary worry since as you know many antibiotics produce loose stools

Staphylococcal enterocolitis is characteristically much more severe than simple drug induced diarrhea and usually is associated with fever However all other things being equal if a patient under these circumstances gets diarrhea I think one should stop

the antibiotic being given unless it is necessary to preserve his life

The stool culture is usually teeming with coagulase positive hemolytic staphylococcus aureus The treatment primarily consists of discontinuing the antibiotic which has selected this resistant agent to replace the normal bowel flora Secondly comes the replacement of fluid and electrolytes and the treatment of shock if necessary since these people often have disturbances of their fluid and electrolyte metabolism by reason of their original illness

Finally and probably least important although it would take a brave man to neglect it is the treatment of the staphylococcal infection itself This should be some agent active against the staphylococcus currently present in your hospital and if for instance erythromycin is active against your hospital staphylococcus it should be the drug of choice Chloramphenicol also is active against a rather large number of so called hospital staphylococci One might also use novobiocin and one could perhaps in addition give neomycin or kanamycin orally I must again emphasize the important feature is prevention of this disease wherever possible

There is another variety of superinfection also probably related in most cases to chemotherapy though certainly not invariably so induced Enterocolitis may be due to other organisms than the staphylococcus This seems prone to occur in post operative patients particularly those having had gastrointestinal surgery It can be due to a variety of organisms We have noticed it is often due to Ps aeruginosa so called pyocanea Apparently certain species of proteus can also produce this syndrome and it is likely that other organisms can do likewise If it is related to the administration of chemotherapeutic agents this of course should be stopped and if the etiology can be readily determined then one should select a chemotherapeutic agent active against that organism The catch is of course that there are few agents active against proteus and pseudomonas being for practical purposes limited perhaps to neomycin in the former and polymyxin in the latter

Doctor Grossman will tell you later about the pathogenic

strains of E coli[6] which are now recognized as an important cause of diarrhea in infants and these probably also cause diarrhea in adults

I think we should also for completeness discuss diarrheas due *to amoeba and flagellates and the like in brief I don t think we* have to emphasize the possibility of amebiasis as the cause of acute and chronic diarrhea While we in this area don t encounter it frequently in clinical form it happens often enough particularly in this day of wide travel and I might add particularly in Mexico that this disease must always be considered Parasitologists who have spent their lives in the Orient use stool cytology to distinguish between amebiasis on the one hand whose exudate characteristically is mononuclear and the so called bacillary dysenteries whose exudate is normally polymorphonuclear

There is one brand of diarrhea that I feel has been very much neglected This is a personal matter with me having been a victim along with some of my family and friends and this is diarrhea due to Giardia lamblia You will notice in most textbooks that this is of doubtful pathogenicity I am willing at the drop of a hat to make an affidavit that this is a genuine pathogen and in no mean proportion at least the Mexican variety This produces a *rather striking syndrome which should be rather easily recog* nized The flagellate invades the duodenum and biliary tract Then one has a duodenal ulcer like syndrome associated with a rather miserable diarrhea consisting of large foul bulky stools This can go on for weeks and months The diagnosis is easily made by examination of the stools The treatment as listed in the textbooks where it is even mentioned is Atabrine® The course usually mentioned is five days which I can assure you is inade quate It produces immediate symptomatic relief and is almost as promptly followed by relapse It should be continued for at least eight days and perhaps longer given in doses of 100 mg 3 times a day

We have touched lightly then on the etiology and pathogenesis of our many common diarrheas and some not so common I think we must always bear in mind the many possibilities although most of those who complain of acute diarrhea will have a benign viral variety

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DIARRHEA IN THE YOUNG CHILD
PROBLEMS IN MANAGEMENT

Moses Grossman M D *

THE most common complaint seen in the younger age group relative to the gastrointestinal tract is diarrhea It also remains one of the more serious diseases of infants Figure 1 shows that although the death rate from diarrhea has decreased in the United States in other countries it still remains very high In addition a startlingly large percentage of the exposed infants succumb in epidemics which occur in newborn nurseries

Diarrhea can be defined as a condition in which an increased volume of stools is produced by hypermotility of the gastrointestinal tract resulting in a loss of water and electrolytes which can be very detrimental to the infant

As with many other biological phenomena it is sometimes hard to know where normality ends and where pathology begins For example a breast fed baby will have more stools normally and they will be more liquid than those of a bottle fed baby The type of feeding an infant receives will determine to a great degree the number and consistency of his daily stools

Figure 2 shows the mean figure accompanied by the standard deviation for the number of stools passed by a healthy infant Note that a four day old infant can have as many as 10 stools within the limits of a mean plus 3 standard deviations

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* Assistant Professor Department of Pediatrics University of California School of Medicine San Francisco

CAUSES OF DIARRHEA

Most of the infectious diarrheas have been discussed by Dr Henry Brainerd and I will not consider the problems of Salmonella Shigella or the viral and parasitic diarrheas which occur in pediatrics as they do in adult medicine These specific infections of the gastrointestinal tract may be particularly severe on oc

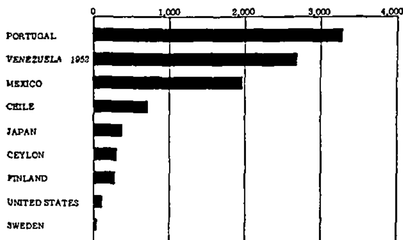


Fig 1 (From Current Status of the Infant Diarrhea Problem *Ann paediat fenn* 3 677 690 1957) With permission from Myron E Wegman M D

casion and in the very young may be accompanied by considerable toxicity One infectious problem however is unique to pediatrics the enteropathogenic E coli It is important to think of this infection and to recognize it because (a) these particular E coli are indistinguishable on an eosin methylene blue agar plate from the normal flora of the bowel (b) these infections cause epidemics in infancy particularly among the newborn (c) they carry a high mortality and (d) specific treatment is available for them—namely neomycin In babies under six months

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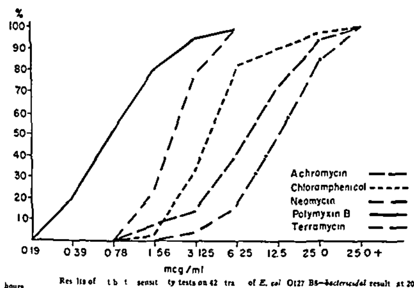
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TABLE II

ENTEROPATHOGENIC E COLI

055 B5
0111 B4
026 B6
086a B7
0112a
0112c B11
0127 B18

demic outbreak it would seem important to look for this as a cause This means that the laboratory has to be prepared to do serotyping of E coli If enteropathogenic E coli are found



Results of antibiotic sensitivity tests on 42 strains of *E. coli* O127 B8—*bactericidal* result at 20 hours.

Fig 3 (With permission from Merlin L Cooper M D to reproduce from his article Escherichia Coli Associated with Infantile Diarrhea in *Ann N Y Acad Sc* 66 78 89 Aug 10 1956)

neomycin can provide very effective therapy Fig 3 shows the results of antibiotic sensitivity tests and compares neomycin with other antibiotics

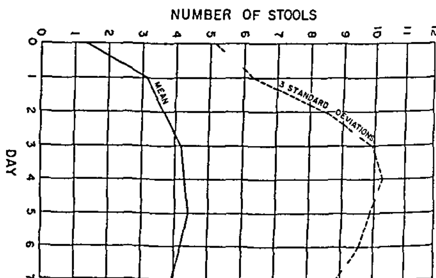


Fig 2 (With permission from Horace L Hodes M D to reproduce from his article The Etiology of Infantile Diarrhea in *Adv in Pediatrics* *8* 13 52 1956)

these infections are far more common than is sometimes recognized

Table I gives the experience at Childrens Hospital of Michigan and indicates that out of 460 cases of diarrhea in infants 106 were due to enteropathogenic E coli whereas only 10 were due to Salmonella 4 to Shigella The E coli were serotyped on the

TABLE I

CHILDRENS HOSPITAL—MICHIGAN
ENDEMIC DIARRHEA IN INFANTS OCT 54—JUNE 55

Total cases	460
Enteropathogenic E coli	106
Salmonella	10
Shigella	4
Undetermined E Coli present— non pathogenic	287
Undetermined	52

basis of their O H and K antigens and seven types (Table II) were considered to constitute the enteropathogenic group

In instances of diarrhea in small babies particularly in an epi

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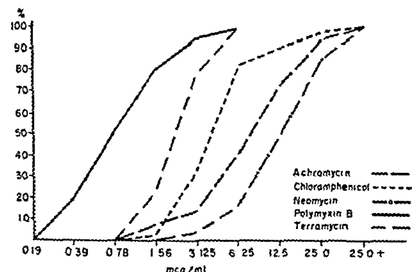


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We might now consider some causes of diarrhea other than infection

Overfeeding is a quite common cause of the milder degrees of diarrhea While not resulting in profound dehydration it does produce a great number of malodorous stools Improper formula with increased fat content or more than comfortable amounts of formula can produce this condition Taking a careful feeding history from the mother will usually make the diagnosis clear

Parenteral diarrhea, which is commonly placed high on the list of causes of diarrhea in small children is actually not very common Although otitis media or pneumonia can be accompanied by diarrhea the latter is seldom the presenting symptom and is in fact no more common than other gastrointestinal symptoms accompanying respiratory infection The principal reason for keeping it in mind is to emphasize the fact that the child who has diarrhea like any other sick child is entitled to a complete physical examination Parenteral diarrhea may also represent a combined respiratory and intestinal infection by one of the ECHO viruses

Metabolic Diarrhea In this group are those babies who are intolerant to a particular food substance The classic example is celiac disease where a specific intolerance to gluten exists and where elimination of wheat from the diet corrects the bulky fatty foul smelling stools Fibrocystic disease is another enzymatic disorder where decreased pancreatic function interferes with the proper digestion of food There is a large group of similar conditions in which fat and carbohydrate are poorly tolerated by the child

Milk allergy is not an uncommon cause of diarrhea Usually this is associated with abdominal pain or colic with bloating and with vomiting *It is a difficult diagnosis to establish* It is also difficult to be sure whether in any given patient the problem is milk allergy or milk intolerance The presence of an allergic family background should be determined Further diagnostic aid might be obtained by finding eosinophils in rectal mucus The best way to explore this possibility is by elimination of milk from the diet for a period of time

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than chloride some of them have more potassium than others

In calculating the amount of electrolytes and water that should be given a good scheme is to replace (1) the estimated deficit (2) the daily requirement and (3) the continuing losses from the gastrointestinal tract There are many ways of handling the calculations Complicated schemes are not recommended What ever scheme one uses it should be simple enough to apply without the use of a slide rule or tables of data

USE OF ORAL ELECTROLYTES

The standard way of treating diarrheas at home has been to have the mother give the baby small amounts of clear water

TABLE III

Composition of Solutions for Parenteral Administration

	(mEq/liter)		
	Na	Cl	K
Normal saline	150	150	0
M/6 Na lactate	167	0	0
1 2 3 solution	76	49	0
1 part M/6 solution			
2 parts 0.85% NaCl			
3 parts 5% glucose water			
Lactate Ringer (Hartmann)	131	107	4
Darrow's	122	104	35
Plasma	145	100	5

Since the loss was not only that of water but also of electrolytes it was felt that it might be wise and might forestall hospitalization in the future if the mother were to administer electrolytes while giving the water This resulted at first in the advice that a certain amount of salt and sugar be added to the water and then led to the use of various prepared oral electrolyte solutions The composition of some of these is shown in Table IV

As experience in the use of oral electrolytes has become greater several problems in their use have become apparent

(1) Electrolytes are sometimes used orally in a severely dehy

stool might lose from 10 to 50 cc of water 10 stools could lose 500 cc of water This amounts to 10% of an 11 pound babys water content Generally speaking in the small infant 5% dehydration begins to be serious 10% dehydration is very serious and requires hospitalization and intravenous therapy 16 or 17% dehydration is usually fatal

The presence of severe dehydration—sunken eyes sunken fontanelle poor skin turgor diminished amount of saliva—may be quickly recognized in a severely dehydrated baby A very helpful thing in estimating the degree of dehydration is the weight decline Daily weighing will give a very good progress report Absence of urine is also helpful but is sometimes obscured by the fact that one does not know whether the diaper is stained with urine or diarrheal stool

FLUID AND ELECTROLYTES

In a general way if a child is dehydrated enough to require parenteral fluids and electrolytes these should be given by the intravenous route and not by hypodermoclysis This latter is the lazy man s way of giving fluids It is much less effective and sometimes harmful in that it delays proper therapy

Stools are almost always hypotonic and as a general rule a baby with diarrhea and resultant dehydration should be given more water than electrolytes The solutions should be approximately one half isotonic

In a baby whose loss of electrolytes is due entirely to diarrhea more sodium is lost than chloride so that replacement solutions should give more sodium than chloride In the treatment of diarrhea physiologic saline is an unphysiological fluid

Darrow and many others have focused our attention on the importance of potassium in diarrheal states and the difficulty in correcting the child s state without the administration of potassium However potassium should never be given until the child is urinating

Table III shows the composition of solutions for parenteral administration which are commonly used in treatment of infants with diarrhea They are all hypotonic and all contain more sodium

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TABLE IX

ELECTROLYTE COMPOSITION OF ORAL FLUIDS

	(mEq/liter)	
	Na	K
Skim milk	20	40
Half strength skim milk	10	20
Breast milk	6	10
Evaporated milk	20	24
Orange juice	0	40
Lytren	50	20

drated child when they should have been given parenterally. Oral fluids are useful only in the prevention of disturbed water and electrolyte balance not in its correction. Thus oral electrolytes might be suitable in cases of mild diarrhea or in the more severe cases after balance has been restored by parenteral means.

(2) Sometimes the mother feels that if a little medicine is good more is better. Administration of more than the prescribed amount of oral electrolyte solutions associated either with further administration of milk or skimmed milk—which is high in solute—or with temporarily decreased renal function due to prerenal azotemia can result in a serious hypernatremic state. These states are seen more frequently in clinical pediatrics of late and are often associated with improper use of such solutions. Children whose diarrhea has been complicated by hypernatremia are sicker, not uncommonly have central nervous system manifestations and are certainly very much harder to treat.

TO FEED OR NOT TO FEED

The conventional manner of treating severe diarrheas has been to starve them. There is no question that the most effective and most rapid way of decreasing the number of stools is complete starvation. Chung and Holt have done a great service in pointing out the great dangers which are inherent in continued starvation. The baby who has been starved a day or two will have frequent soft green stools upon attempted feeding; these are really starva-

tion stools Unless *their nature is recognized* further starvation may proceed with depletion of energy reserves decrease in the child's resistance and sometimes result in death Holt and Chung further showed that feeding babies with diarrhea who were not vomiting resulted in a net gain rather than loss of fluid although the number of stools per 24 hours was increased The babies retained more fluids than they lost by the gastrointestinal route They suggested that infants with diarrhea be fed This recommendation was not completely accepted because it was somewhat misinterpreted

In the first place some physicians who took it as license to feed babies with severe diarrhea counted the fluid they took by mouth as total fluid intake This did not work out well at all A severely dehydrated child whether it is fed or not should receive the required amount of fluid parenterally

In the second place whether a child is at home or in the hospital the mother looks for therapeutic results in terms of decrease in the volume of diarrheal stools Besides pleasing the mother there are other advantages in arresting the diarrhea more rapidly —diminished irritation of the buttocks and possibly shorter hospitalization. Feeding is likely to increase the duration of the diarrhea Starvation therefore has certain merits but no child should ever be starved more than 24 hours no matter what happens to the stool

DIETARY REGIMEN

Following initial starvation boiled skimmed milk is often used to start feeding in diarrheal states Recently this method has come under question because of the *problem of hypernatremia* Skim milk is a high solute fluid and in a dehydrated child it may present an overload of solutes for the kidney to create resulting in hypernatremia Half strength boiled skimmed milk would be the answer to this objection An immature gastrointestinal tract which has been irritated by a few days of diarrhea is capable *apparently of passing through* undigested protein this possibly could make a child allergic to milk Tough milk curds may also be somewhat irritating For these reasons one might give some

thought to the use of other products such as soybean, nutramigen, banana formula or meat base formula

DRUG THERAPY

Finally we might consider the use of drugs in therapy Dr Brainerd has covered the use of drugs in the treatment of Shigella, Salmonella and parasitic infections His remarks are applicable to children as well as adults As has been mentioned previously, neomycin is the drug of choice in the treatment of enteropathogenic E coli The dose is 100 mg/kg/day by mouth It is barely absorbed and has a minimum of untoward effects Needless to say it is of no help whatsoever in the treatment of the common viral diarrheas

Various pectins are commonly used to bind the stool Apple in various forms including powder falls in this group since it contains as much pectin as a number of common preparations These drugs do no harm do bind the stools somewhat but really exert very little influence on the course of the diarrhea except to make the mother feel that something is being given

Paregoric which is so useful in the treatment of adult diarrheas has very little place in the management of the infant or young child It seems rather hazardous to let the mother have paregoric at home—again for the reason that she might think that if a little medicine is good more is better Phenobarbitol and belladonna are often used to decrease gastrointestinal motility They have some slight effect in this respect but are really more useful and effective if cramps are a presenting problem

Finally it has been shown that the child may have fairly significant hypoprothrombinemia following a prolonged diarrheal state For that reason prolonged diarrheal state should probably be followed by the administration of Vitamin K

CONCLUSIONS

This has been a very rapid survey of some of the problems which are encountered in the management of diarrhea in the very young The points which I have tried to emphasize have been

(1) the recognition of epidemics of enteropathogenic E coli (2) the recognition and proper parenteral treatment of dehydration and finally (3) the occurrence of the hypernatremic state in diarrhea and its prevention

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REGIONAL ENTERITIS

HUGO C MOELLER MD PH D *

Regional enteritis is a disease manifested by pronounced increase in intestinal motility It is characteristic therefore that patients having this disease complain of diarrhea and abdominal cramps Although the medical historian Hyman I Goldstein traced descriptions of cases back to Morgagni in 1761 it was not until 1932 that Crohn published his classic study describing the fundamental clinical picture of this disease [10, 24] In addition to the common complaints of diarrhea and abdominal cramps fever loss of weight anemia perianal abscesses and fistulas are frequently found Occasionally a mass in the right lower quadrant is palpable Pathologically the lesions in the intestine are characterized by a granulomatous necrotizing ulcerating and cicatrizing process frequently accompanied by fistulas arising from the lesion in the small bowel and extending either to the neighboring viscera or to the abdominal wall

Crohn used the name terminal ileitis to describe the first 14 cases he reported Although the terminal ileum is involved in 80% of the cases the present pathological concept of enteritis recognizes a more widespread distribution of the lesion throughout the gastrointestinal tract [3, 4, 1] At present the accepted term for this disease is regional enteritis [0, 31]

INCIDENCE

The exact incidence of regional enteritis is unknown although modern techniques have increased the frequency of diagnosis It seems to occur at any age In a study of 600 patients at the Mayo Clinic the age at onset varied from 4 to 74 years how

* Assistant Professor of Medicine University of California San Francisco

ever in 76% of the patients the disease first appeared between the ages of 11 and 35 [7] Familial susceptibility seems to be a definite factor in its occurrence The sex incidence is not significant

ETIOLOGY

The etiology of this disease remains unknown The multiplicity of the theories advanced indicates the unsettled nature of this problem Bacterial protozoal and viral agents have been considered in turn as have sarcoidosis allergy trauma and emotional factors Since the chief pathologic feature of this disease is a noncaseating tuberculous granuloma tuberculosis was long considered to be a causative factor However reinvestigation of this problem by laboratory cultures and animal inoculation seems definitely to rule out tuberculosis

A recent description from Denmark of ileitis in pigs suggested an anatomical distribution similar to man's and pointed to the possibility of using a laboratory animal for the study of this disease [11] A type of ileitis has been described in cocker spaniel dogs [6] Up to the present time no causative agent has been identified nor has it been possible to transfer the disease experimentally Although there is a close similarity between the pig ileitis and regional enteritis in man a histologic study reveals absence of giant cells and tubercles in the porcine ileitis

Since the histologic picture in regional enteritis is similar to sarcoidosis there has been much speculation as to whether the two conditions are identical However patients with sarcoidosis rarely have an involvement of the small bowel and the disease is not associated with the appearance of fistulas or with rectal complications [3]

Because many patients with regional enteritis have found that foods such as milk aggravate their condition it has been hypothesized that allergy or hypersensitivity is a causative factor [3] This theory has not as yet received general acceptance and proof of this hypothesis is limited by the methods of research in the field of allergy

The characteristic pathologic feature appears to be lymphangitis Lesions resembling ileitis have been produced by feeding animals finely divided silicates These experiments are signifi

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because of pressure on the arterial lumen The secondary changes consist of ulceration cicatrization and stenosis which may dominate the microscopic picture and obscure the primary specific features that give rise to them

Recently there has been interest in the aberrant pyloric glands resembling the Brunner type of mucus producing glands, which have been found in over 80% of patients with regional enteritis [17,19] The significance of this finding is not immediately apparent and more studies must be done to confirm and extend this observation

SYMPTOMATOLOGY

In a discussion of its symptom complex regional enteritis must be considered separately as acute enteritis and chronic enteritis Acute enteritis is manifested by diarrhea abdominal cramps fever local abdominal tenderness usually in the right lower quadrant and leukocytosis All the signs and symptoms of acute appendicitis may be present and occasionally surgical intervention is necessary to eliminate the possibility of acute appendicitis *Chronic regional enteritis is manifested by intermittent cramps* right lower abdominal pain diarrhea fever malnutrition palpable abdominal mass loss of weight fistula formation occult blood in the stool and leukocytosis In severe cases steatorrhea multiple vitamin deficiencies and electrolyte disturbances may occur

DIAGNOSIS

The x ray examination is the most important diagnostic procedure The string sign is characteristic and was first described by Kantor it results from the narrowed lumen of the terminal ileum [16] *This sign is one of the first x ray characteristics of the* disease to be recognized but it is not pathognomonic of regional enteritis because it may also appear in ileocecal tuberculosis and sarcoma The string sign usually indicates however that the disease has been present for a long time It represents severe stenosis and cicatrization of the wall of the bowel Marshak and Wolf [1] found that the earliest changes in the course of the disease *are blunting and thickening of the mucosal folds* With further progression of the ulcerating process the mucosal pattern disappears and the bowel becomes rigid There may be post stenotic dilatation and fistula formation from bowel to bowel

cant because results seem to indicate that materials within the intestinal stream may enter the lymphatic system and set up an inflammatory reaction

In the vast majority of patients the initial disease is in the terminal ileum Diversion of the fecal stream by a short circuiting operation is often followed by regression of the process in the excluded areas of the intestine When the disease recurs in a patient who has had a resection, it is usually localized in the new terminal ileum These observations suggest that there may be some agent present in the intestinal stream which initiates the disease process There may be more than one such agent

The role of abdominal trauma in the initiation of regional enteritis is difficult to determine although there are many patients whose clinical histories suggest such a causative factor [7]

Bacterial protozoal and viral agents have been thoroughly studied So far none of these has been demonstrated to be the causative agent and the possibility of a bacterial basis for the disease probably has been eliminated However the theory of a viral origin has not been completely discarded Modern virology may give a partial answer to this problem

There seems to be no immediately apparent personality profile associated with appearance of the disease although no large groups have been thoroughly studied from a psychoanalytic point of view [6, 13]

PATHOLOGY

Most observers accept regional enteritis as a distinct clinical entity but there is some dispute as to its pathologic specificity Detailed studies by Hadfield Warren and Rappaport have demonstrated the characteristic histologic features of the disease Hadfield stressed the localized submucosal lymphoidal hyperplasia with formation of noncaseating giant cell tubercle like systems [14] Warren and Rappaport [8] pointed out that these are primarily localized in the proliferating endothelial cells within the lacteals This proliferation gives an initial picture of structural lymphangitis The mucosal involvement is a secondary phenomenon The primary lymphangitis with eosinophil and lymphoid cells forms a conglomerate mass of giant cells These primary changes result in inflammation and fibrosis possibly

Surgical Approaches

The type of surgical intervention is still a controversial sub ject The original approach consisted of excision of the inflamed portion of the bowel This was founded on the sound surgical principle of removal from the abdominal cavity of the obviously pathologic bowel Subsequently an exclusion or short circuiting type of operation became widely used The surgical mortality was somewhat less in the one stage procedure and recurrence rate probably no greater than that following primary resection Occasionally upon re entering the abdomen for an elective resec tion of the previously involved bowel the surgeon would find marked resolution of the active process This observation added *further support to the short circuiting operation as the surgical* treatment of choice

The relative merits of the accepted methods of surgical treat ment are difficult to evaluate since the results are subject to various interpretations and differ considerably in clinics employing similar techniques It is however generally agreed that transec tion of the ileum above the affected loop of bowel is imperative The aim is to localize the lesion and to prevent extension of the disease The type of ileocolic anastomosis varies with the surgeon

Medical Treatment

Since the etiology and pathogenesis of the disease are as yet unknown all attempts at medical management are strictly sup portive In general the regimen should provide (1) rest (2) adequate nutrition with a high caloric low residue diet (3) anti diarrheal medication (4) control of infection by antibiotics and chemotherapeutic agents and (5) replacement of blood

Rest both physical and emotional is an important factor in the treatment of a patient with regional enteritis During the acute phase complete bedrest with only bathroom privileges is indicated Although there may not be a specific psychogenic basis for regional enteritis the emotional state of the patient must be carefully evaluated A sound physician patient relation ship is important in the treatment of this long standing debilitat ing illness Mild sedation phenobarbital 15 to 30 mgs four times daily is often necessary to help the patient get needed rest Tran

bowel to abdominal wall small bowel to rectum bowel to bladder or bowel to vagina

Recently attention has been focused on a form of enteritis called combined ileocolitis [20] Yarnis uses the term to denote the presence of granulomatous ileitis and non specific ulcerative colitis, two separate and distinct pathologic processes in the same patient It is generally accepted that approximately 20 to 40% of patients with ulcerative colitis have a backwash ileitis that can be distinguished pathologically from primary regional enteritis There is mucosal ulceration with distensibility rather than thickening and rigidity characteristic of enteritis Very rarely there may be simultaneous involvement of the terminal ileum and the colon with a disease which has the pathologic picture of regional enteritis In view of the association of the two disease entities it is essential to perform a barium enema examination in every patient who has regional enteritis

THERAPY

Acute Enteritis

If the abdomen of the patient with acute enteritis has been opened because the disease could not be distinguished from acute appendicitis it is felt best at the present time to do nothing except possibly a prophylactic appendectomy if the cecum is not involved The incidence of fistula formation has not been increased significantly in those patients who have had the operation [9] Postoperative care should be directed toward treatment of the ileitis

Recurrent and Chronic Stenosing Enteritis

Therapeutic procedures are difficult to evaluate because of the present lack of knowledge regarding the natural course of the disease Originally surgery was assumed to be the treatment of choice However the rate of recurrence of the disease has been reported as high as 63% At the present time the indications for surgery are usually complications of the disease such as (1) stenosis with obstruction (2) fistulization to other loops of the bowel to the bladder to the vagina or to the skin (3) the presence of a large tender inflammatory mass or (4) bleeding [8] If these complications do not appear the conservative approach to the disease is at present preferred

regional enteritis is salicylazosulfapyridine (Azulfidine®). This is administered 1 gm every three hours during the acute phase of the disease. Its mode of action is probably local and anti-inflammatory. Later the dosage may be reduced to 1 gm 4 times a day. Occasionally, side reactions such as headache and nausea occur. This is managed by stopping the drug temporarily and reinstituting it in a smaller dose.

Transfusions are necessary for many patients since they have been losing blood chronically. It is of great help to restore the individual's sense of well-being, thereby increasing the appetite and general nutrition.

In patients who do not respond to the above outlined conservative approaches, treatment with corticotropins or corticoids should not be withheld. Since no treatment of regional enteritis has been wholly satisfactory and since corticoids have been demonstrated to be useful in the treatment of other granulomatous processes, it has been hoped that these compounds would influence the course of regional enteritis. Varying results of corticoid and corticotropic therapy have been reported.[18, 20, 24] Often the administration of corticoids may be followed by dramatic remission of fever, diarrhea and weight loss. For the patient who is acutely ill, Acthar® gel 40-80 units per day or intravenous corticotropins can be used for approximately two or three weeks. A corticoid administered orally may then be instituted. Meticorten®, Medrol® and Decadron® have all been used. The dosage is determined by the minimum amount necessary to maintain the patient in remission and to prevent the side effects associated with the administration of corticoids. These patients may need corticoids for a long period of time, perhaps for life. The x-ray appearance of the involved bowel does not reflect objectively the clinical response.

Bargen advocates the use of x-ray therapy to the abdomen as an important adjunct to the management of regional enteritis.[1] This form of treatment is at present under investigation in various medical centers.

SUMMARY

Regional enteritis may be regarded as a distinct clinico-pathologic entity, many times associated with increased gastrointestinal

quilizers (Equanil® Sparine® and Suavitil®) are valuable to control the activity of anxious patients In order that the patient get some restful sleep barbiturates such as Tuinal® or Nembutal® may be used

A bland low residue high caloric diet with lean meat and advoidance of fruits and vegetables should be instituted in the early phase of acute enteritis The food should be nutritious and attractively prepared After the acute phase has subsided well cooked fruits and vegetables may be added Highly seasoned irritating foods must be avoided Occasionally the removal of wheat eggs milk and milk products may be necessary if the patient has a specific intolerance to these products If the disease is of long standing stearrhea may occur Fat restriction may be necessary Occasionally a gluten free diet is helpful

Supplementary vitamins should be given Large doses of the B Complex vitamin may be necessary Occasionally liver extract and vitamin B_{12} must be given parenterally particularly if there is extensive involvement of the bowel If there is prolonged steatorrhea parenteral injection of vitamin K may be necessary to reduce the prothrombin time Iron may be necessary but it is best supplied parenterally as Imferon®

Antispasmodics and sedatives are most useful in controlling the acute diarrhea Atropine sulfate 0 43 mgs four times daily Pamine® (methscopolamine) 2 5 mgs four times daily and BE pH AN® one tablet twice a day are antispasmodics of choice Occasionally opiates such as tincture of deodorized opium 10 drops four times a day may be useful Kaolin pectin bismuth and methyl cellulose may aid in controlling the diarrhea A mixture of equal portions of calcium carbonate and bismuth subcarbonate may be given 2 gms every two to three hours

Antibiotics and chemotherapeutic agents are useful in the treatment of some patients possibly in reducing the risk of secondary bacterial infection in the intestine and in controlling some of the external fistulas Penicillin and dihydrostreptomycin are probably the most effective antibiotics However some antibiotics may actually aggravate the diarrhea by changing the bacterial flora in the bowel They should therefore be used sparingly

A very useful chemotherapeutic agent in the management of

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motility Since the etiology is unknown therapy remains empirical Conservative medical management is the treatment of choice in acute enteritis because there is a possibility of spontaneous resolution A certain percentage of patients will develop recurrent chronic enteritis Surgery will become necessary if complications such as fistulization bleeding obstruction or an abdominal mass occur Most medical regimens are supportive and include a high caloric low residue nutritious diet antispasmodics and occasionally antibiotics The chemotherapeutic agent, salicylazosulfapyridine (Azulfidine®) corticoids and x ray therapy to the abdomen also have been helpful in managing this serious disease

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and was to be evaluated as a possible candidate for surgery

Her first symptoms occurred in 1951 before this time the patient had considered herself in excellent health Diarrhea began in October 1951 and was characterized by 3 to 4 loose brown stools each day accompanied by cramping in the lower abdomen The patient was admitted to Oak Knoll Hospital in 1951 where her stools were examined and a proctoscopic examination done She was told that she had an irritable bowel and was discharged with prescriptions for a high protein low residue diet and an "antibiotic

Intermittent bouts of diarrhea occurred and blood appeared in the stools during the first trimester of her only pregnancy In February 1952 she was admitted to the hospital for toxemia of pregnancy 6 days prior to delivery The delivery was uneventful and the patient was discharged in 5 days

On December 28 1953 the patient was admitted to the U S Naval Hospital at Coronado California complaining of 1) diarrhea (an average of 10 bloody stools a day) 2) fever 3) chills 4) loss of appetite 5) weakness and 6) 30 pound weight loss A letter from the physician who attended her at that hospital stated that the patient ran a high fever and passed approximately 20 bloody stools per day during the first 2 weeks of her 6-week stay in the hospital Initial therapy consisted of fluids given intravenously antispasmodics sedatives vitamins and Talamyd® (phthalyl sulfacetamide) After a few days ACTH 20 units daily given intravenously was added Following the latter therapy her fever resolved her appetite returned stools decreased in number to an average of 4 per day and were not bloody Later the patient was treated with Terramycin® During her hospital stay she developed almost persistent rectal pain and an anal fistula was found which drained purulent material She was discharged on February 5 1954 Her regimen consisted of cortisone 50 mg daily to be taken for two weeks then to be dropped to 25 mg daily for another two weeks and then to be discontinued ferrous sulfate 0 3 gram three times daily vitamins and a high protein high carbohydrate diet

The patient responded well to this regimen but she had a

SYMPOSIUM ON ULCERATIVE COLITIS

Moderator

J Arnold Bargen M D

Professor of Medicine Mayo Foundation

Panel Members

Lester R Dragstedt M D Ph D Professor of Surgery University of Chicago School of Medicine

John M Elliott M D Assistant Clinical Professor of Medicine University of California School of Medicine San Francisco

Leon Goldman M D Professor and Chairman Department of Surgery University of California School of Medicine San Francisco

Harold M Hand M D Associate Clinical Professor of Medicine University of California School of Medicine San Francisco

Gordon McHardy M D Associate Professor of Medicine Louisiana State University Medical School

Alfred L Schmitz M D Assistant Professor of Radiology University of California School of Medicine

Case Presentation

Beatrice Berteau M D Fellow in Gastroenterology University of California School of Medicine San Francisco

Dr Bargen This will be an informal discussion Dr Berteau will present the patient whose case we are to discuss

Dr Berteau L B a 26 year old white married woman entered the University of California's Outpatient Department for the first time in February 1957 She had chronic ulcerative colitis

noted No abnormalities were found upon neurological examination.

Proctoscopic examination could be done only up to 12 cm Scarring of the posterior anal wall a result of the previous operation was noted The rectal mucosa was granular and friable Two hypertrophied papillae were seen at the ano rectal junction There was no spontaneous bleeding from above and there was no evidence of pseudo polyps

A barium enema examination on February 20 1957 showed evidence of shortening narrowing rigidity and pseudopolyposis The mucosal pattern of the terminal ileum was also abnormal An increase in the shortening and narrowing of the colon was noted in comparing this film with films taken September 21 1956

A small bowel series of films taken on March 8 1957 revealed no abnormalities until the terminal ileum was reached where narrowing of the lumen and irregularity of the mucosa were seen

Routine laboratory tests done on February 20 1957 gave the following results hemoglobin 12 1 RBC 4 01 WBC 5 920 with a differential of PMN 66% lymphocytes 25% eosinophils 3% monocytes, 6% Sedimentation rate was 10/mm/hr (Wintrobe) Six white blood counts taken at intervals over a period of 15 months were always normal In June 1958 the hemoglobin was 13 4 grams

Therapy has consisted of a bland low residue diet Meticorten® 5 mg twice daily Azulfidine® 1 gram three times daily phenobarbital 30 mg three times daily and Pamine® 2 5 mg three times daily

As a result of following this regimen the number of the patient s stools decreased to an average of 2 daily Rectal urgency and incontinence however required additional therapy with *prednisolone* suppositories *10* mg daily for about *6* weeks As the patient s condition improved the dosage of Meticorten® was gradually reduced and finally discontinued in September 1957 The patient continued to do very well A month later the daily dose of Azulfidine® was likewise decreased to one half the original amount Slight rectal urgency recurred in March 1958

relapse in August 1954, after discontinuation of therapy A remission ensued upon reinstitution of strict management and at that time she was operated upon for the anal fistula

The patient had another recurrence of bloody diarrhea and was seen by a physician in Merced California in April 1955 She was hospitalized for 4 days and improved quite markedly on a regimen of Hydrocortone® 20 mg three times a day isoniazid 100 mg three times daily Thorazine® 25 mg twice daily a low residue diet and injections of ACTH 80 units every 3 days Therapy as outlined was continued intermittently during the following 22 months but progression of the disease was evidenced by passage of 8 to 9 stools daily rectal urgency and some incontinence Furthermore upon administration of a barium enema (at Merced California on September 21 1956) radiologic evidence of ulcerative colitis involving the entire colon with a suggestion of pseudo polyps in the transverse colon and in mucosal irregularity involving the terminal ileum was seen

In February 1957 the patient was referred to the University of California Hospital Her past history was noncontributory She denied having any allergies and mentioned no symptoms referrable to her joints eyes or skin

Physical examination at this time revealed a chronically ill appearing white woman who weighed 112 pounds Her temperature was 98 8 F pulse was 88 full and regular Respirations were 20/min Blood pressure was 120 70 The skin and eyes were normal Funduscopic examination revealed nothing remarkable Ears nose and throat appeared normal No abnormalities were noted in the neck and no abnormalities were noted in the breasts Excursions of the diaphragm were equal bilaterally there were no evident bony deformities in the chest The lungs were clear to percussion and auscultation The heart was not enlarged no murmers were audible A regular sinus rhythm of 88 per minute was noted

The abdomen was normal in contour no organs or masses were palpable Slight generalized abdominal tenderness without rebound was present No abnormalities in the extremities were

A No

Q Why?

A I don t particularly like milk

Q Have you ever been known to have any trouble when you drank milk?

A Yes The last week I was here they gave me some milk and it didn t agree with me At first they had me off milk completely

Q Do you know of any food producing bowel upsets other than milk?

A Sometimes candy if I eat too much

Q Do you drink milk now?

A Once in a while

Q Does it still upset you?

A No not like it used to

Q Do you eat salads?

A Every once in a while

Q Did you dislike these when you were a girl?

A Yes

Dr Bargen The introductory paragraph of her history states that this lady was brought to the out patient department as a candidate for possible surgery I should like to get the opinions of members of the Panel about her future therapy the nature of her illness and some comments as to how this case compares to the average patient with ulcerative colitis

Before doing this I think we should have Dr Schmitz show us the original films While he is doing that may I ask the surgeons if they would have operated when they first saw her

Dr Dragstedt I think perhaps I would I must confess that I am quite surprised to see this excellent result It may be because in our clinic the patients with this disease that have been referred to me for surgery look like they just got out of an Egyptian tomb They are in the last stages of their disease and I am reluctant to operate on them I think perhaps I would have taken the opportunity here to see if surgery in the early stages of the disease could do something more than when we operate in the final stage of the disease when there is nothing left for us to do but total colectomy

At this time citro flavonoid ascorbic acid compound * 2 capsules three times daily was prescribed Since the symptom of rectal urgency was mild in degree the gradual reduction in Azulfidine® dosage was continued and in April 1958 the drug was discontinued Approximately 7 weeks later the patient developed cramping abdominal pain and diarrhea without blood (5 to 6 stools per day) Azulfidine® was again given 1 gm every 3 hours for 10 days The results were excellent and she again had only 1 or 2 normal stools per day Maintenance doses of Azulfidine® 0 5 grams four times daily have been continued to the present time

The patient weighed 113 pounds in February 1957 In November 1958 she weighed 130 pounds and was feeling well X rays of the colon taken in November 1958 will be shown

Dr Bargen We shall now ask this lady a few questions Some of you might like to know whether she is awakened at night to have bowel movements

A Yes

Q When did you first have stools at night?

A Since the beginning

Q How many stools a day are you having at the present time?

A One most of the time Every once in a while I have two

Q Have you seen any blood in them recently?

A No

Q How long have the stools been free of blood?

A I dont remember

Q Do you still have any cramping?

A No

Q Are you restricting your diet in any way?

A No I guess it has been about six months now that I eat anything I want However I dont go overboard on fried foods I dont particularly like them

Q Is that one thing that is forbidden in your diet?

A Yes

Q Do you drink milk?

---

* Supplied as C V I ® by U S Vitamin Corporation



Figure 1

denced by the mucosal irregularity The next examination five months later shows definite progression (Fig 2) We have more contraction and the recto-sigmoid colon is straight The pseudopolyposis is again demonstrated At this time the patient had a small bowel series which was negative with the exception of the changes previously seen in the terminal ileum

Dr Bargen The first part of the second paragraph of this patient's history doesn't tell us a great deal of interest except that the trouble began in October of 1951 when she had only three or four loose watery stools and she was said to have an "irritable bowel syndrome"

Now the next question that comes to mind concerns the thing

Dr Bargen What would you have done in this case?

Dr Dragstedt Thirty years ago the common operation performed in patients with severe chronic ulcerative colitis was end ileostomy I have seen many patients with the severe form of the disease make a remarkable recovery when the fecal current was diverted from the colon The temperature returned to normal blood disappeared from the stools and anemia improved and the patient gained weight I must admit however that diversion of the fecal stream never caused the colon to become completely healed It still remains a possibility that if this diversion were done earlier in the disease the result might be better that complete healing might occur and re anatomosis of the bowel performed I must say that I have not been able to do this with a good result in a single patient up to the present time

Dr Goldman I agree with everything Dr Dragstedt said I think it is difficult to look at this young woman who looks so healthy now and say that we would have been inclined to operate on her in 1951 I think that in determining indications for surgery in this disease we first consider those patients who have obvious complications that are urgent indications for surgery In other cases we have to judge them on the basis of the clinical history and sigmoidoscopy and roentgen examination realizing that there can be a discrepancy in the severity in the way these things affect the patient I think that for anyone to say now that we should have operated on her seven years ago when we see a patient as healthy looking as she is today would probably be considered quite an enthusiast for surgery However if we had seen her at the time I think that we may have recommended surgery which as Dr Dragstedt said means an ileostomy and a total colectomy in order to rid her completely of the disease

Dr Bargen I shall not ask the internists to answer the question about surgery now Lets have Dr Schmitz show us the roentgenographic findings and perhaps he will discuss them for us

Dr Schmitz These films are dated September 1956 (Fig 1) There is complete lack of the haustral markings with pseudopolypoid changes in the colon There is a moderate shortening of the large bowel Involvement of the terminal ileum is evi

Dr McHardy I think this is a subject that has caused considerable debate It resolves itself into a question of the individual under consideration at the time The most severe case I can recall was an individual upon whom a therapeutic abortion was done because of ulcerative colitis her physician feared that she would have difficulty resulting from pregnancy She promptly had a severe relapse six weeks after her therapeutic abortion was done I have seen patients who during pregnancy became quiescent and do remarkably well through normal full term pregnancy There is that emotional component that upsets some individuals during their pregnancy to create difficulty at varying periods of parturition I personally do not feel that pregnancy should be used as an indication for therapeutic abortion in chronic ulcerative colitis patients I also feel that quiescent chronic ulcerative colitis and normal pregnancy are compatible

Dr Bargen You have brought up a point that I would like to emphasize Ulcerative colitis may begin during pregnancy and very often if it does so or when present may become quiescent during pregnancy The first indication of this lady s disease was when she had loose stools and passed blood during her first pregnancy December 28 1953 when admitted to the Naval Hospital she apparently had her second attack coming some 22 months later when she was really very ill According to a letter from her attending physician the patient ran a high fever etc The treatment at that time was that in vogue i e the use of some form of sulfa drug and in this case Sulfathalidine® which is one of those drugs that is supposed to have local effects without much absorption It was also at this time that the use of ACTH was begun Dr Hand would you mind saying a few words about the treatment at this point?

Dr Hand This patient was at that time apparently having a very violent flare up of her ulcerative colitis The treatment given at that time was as one would expect general supportive in type In these *fulminant* episodes one has to use almost everything that will support the patient—such as fluids blood transfusions vitamins and chemotherapy In addition one may have to use ACTH I V which I think is proper in these severe cases The



Figure 2

that happened during the first trimester of her only pregnancy. Dr Elliott, what does that make you think of?

Dr Elliott That probably took us back to 1951. It makes me think that pregnancy had something to do with her colitis and this is occasionally the situation. Pregnancy may be associated with the onset of colitis and frequently is in young women. The other thing is that pregnancy often will improve a pre existing case of colitis only to have it occur again after delivery. Thus pregnancy may precipitate ulcerative colitis or temporarily improve it.

may be multiple or they may be single and the presence of a fistula in itself is not necessarily an indication for colectomy You should have other indications for removal of the colon based on other findings This is very common and unfortunately may often lead to fistula but in this case has apparently not done so

Dr Bargen Would you have done a fistulectomy at that time?

Dr Goldman No not at that time I think a patient who has ischiorectal or perianal abscess should be drained and one should not try to find an internal opening at that time Fistula should be excised after the definite ileostomy and colectomy Healing may be impaired if it is carried out during the active phase of the disease It may be corrected during a remission

Dr Bargen Do you agree with that Dr Dragstedt? When do you recommend fistulectomy?

Dr Dragstedt I agree entirely with what Dr Goldman has said The response of this patient to medical treatment surprises me When I saw the first x ray pictures I might have advised diversion of the fecal stream by end ileostomy as a conservative measure With the fulminant episode that developed on the second admission I probably would have recommended total colectomy I must admit that I am surprised that this young lady looks as well as she does We must remember however that she has a functionless colon which is of no use to her except as a passageway for fecal material It probably has no absorptive function and may well be the site of a secondary carcinoma If she gets a carcinoma, she will die of it as this is a very malignant form of cancer She is a pretty girl she has a nice dress but she has a bad colon which is a constant hazard

Dr Bargen I am sure that there are at least four members on this Panel who would disagree with you Dr Dragstedt I'm not going to ask them now I will do that later The question I would like to settle now is whether you would have done a fistulectomy on this patient

Dr Dragstedt Yes

Dr Bargen Later she had a remission and a fistulectomy I think it was probably quite in order to do it at the time it was done If the rectal lining was healed then I think it was justified

ACTH given by slow I V drip over a long period of time say eight hours or so is very striking in its effect and sometimes seems to pull these patients right out of death s arms I think the treatment given at that time of that severe flare up was quite proper and also quite effective

Dr McHardy May I disagree with one point—that the treatment was proper I notice in the first place that she was given some form of antibiotics exact type not stated and at a later period in 1953 she was given Terramycin® I question that the use of a wide spectrum antibiotic in ulcerative colitis is proper treatment Secondly I notice iron sulfate was given These patients often experience an extreme difficulty with such preparations I would be reluctant to give a patient Terramycin® who had ulcerative colitis I would employ parenteral iron

Dr Hand I would agree at least that they should not be given for any prolonged period

Dr Bargen I think we should answer that question equivocally One must see the patient because there are many times when these wide spectrum antibiotics do pull patients through a grave crisis I would agree in general that antibiotics are usually not indicated but I would not say that they never should be used

Dr McHardy Wouldn t your preference be for streptomycin and penicillin instead of the tetracycline group?

Dr Bargen That is correct

During the hospitalization she developed almost persistent rectal pain and then incontinence developed Dr Goldman would you make some comments regarding this complication?

Dr Goldman Patients with ulcerative colitis or any disease that causes a protracted diarrhea is apt to have an acute proctitis or an infection which starts in the rectal wall and may go on to formation of an ischiorectal or perianal abscess These vary in degree and depending on the compartment that is involved they may be very extensive and of course they should be drained as soon as the abscess forms and the drainage is more important than any antibiotic therapy When these are drained they are very apt to be followed by the formation of a fistula The fistula may require further surgery These fistulae in ulcerative colitis

it had been at times in the past I am sure it wasn t 10 when she had the fulminant attack

Dr Bargen That s exactly the point I want to make With these very sick people the sedimentation rate goes to figures which are very high 120 150 mm the first hour by the Wester gren method Dr McHardy what do you think about these leukocyte values

Dr McHardy I don t think they are too unusual This patient was on sulfonamides if I remember rightly straight through and that was controlling most of the secondary bacterial infec tion We have seen normal counts in the most fulminating cases unless these is a massive secondary infection

Dr Bargen Do you agree with Dr Hand about the sedimen tation rate?

Dr McHardy Yes Dr Bargen It is my experience that the leukocyte count might be normal and the sedimentation rate be elevated

Dr Bargen Now then we come to the beginning of the use of Azulfidine® and Dr Elliott why was it started at this time?

Dr Elliott I don t know why it was started at this time be cause you Dr Bargen have been propounding its use for many years but we thought it was a good idea to start it

Dr Bargen It is obvious that there is some difference of opinion about the need and use of this drug and when to use the hormones I did want to bring out the use and indications of this important drug Would any one of you men like to say something about the use of Azulfidine®?

Dr McHardy We use Azulfidine® We have a tendency to vary the drug after a period of time We will keep a patient on Azulfidine® over a period of time and then switch them to another of the sulfonamides Now don t ask me why but it has just been our experience that these patients may have a relapse while they have been on other agents as well as Azulfidine® and therefore I like to alternate it so as not to build up a tolerance to a particular agent I think it has been an entirely satisfactory drug with rela tively few side effects and only the occasional patient has a sul

but I think that the whole answer should depend upon that Fistulectomy in the presence of active ulcerative colitis is ill advised It should be done when the disease is healed

Now then we come to the next attack which is 20 months later, April, 1955 She was hospitalized for four days and improved quite markedly on hydrocortisone etc Now, Dr Elliott I would like to hear from you regarding the use of steroids

Dr Elliott At this time in April 1955 we were in the midst of learning about steroid therapy and of course we still are This case can serve as an example of one way to go about it namely the intermittent use of steroids to control acute attacks Now a good deal of help can be obtained this way These people characteristically and I don t think we can say that this lady s disease is over start off with low grade episodes of diarrhea that steadily worsen If caught early they can be at least cooled down considerably and of course with the more modern steroids such as methylated prednisolone and triamcinolone we are doing it quite effectively on reasonably low doses The point is to start treatment early and have the patient report immediately when any changes occur and to start in what must be called suppressive therapy This is an effective way to my mind of controlling a good many of these chronic cases Any one of these attacks might end up by putting them in the hospital as happened twice with this girl We have had the experience here of being able to modify the acute flare up very successfully I generally add Azulfidine® along with steroid therapy in doses of 4 6 grams a day and will continue this for several months until the process quiets down

Dr Bargen What is normal Wintrobe sedimentation rate? We use the Westergren method

Dr Hand It is about 10 ml hr

Dr Bargen Is that usual for a person with as active ulcerative colitis as this woman has?

Dr Hand I think the sedimentation rate here is much slower than one ordinarily sees To me this would indicate that the acute inflammatory process was not nearly as marked at this time as

program to exact but we have had satisfactory results on such a regimen

Dr Bargen Azulfidine® is a combination of sulfapyridine and sodium salicylate chemically combined and just how it affects the bacteria of the intestinal wall is still somewhat uncertain

Dr Hand Do you think the salicylate radical in this drug may have an anti inflammatory effect much as we see in rheumatic fever?

Dr Bargen Yes that has been my opinion You see this drug came into being about the same time as the steroids but the steroids worked more dramatically so it took a long time for people to learn to use this drug but I am sure if the steroids had not been discovered at the same time that the Azulfidine® was developed we probably would never have used the steroids so freely in this disease Dr Schmitz let us see the last films

Dr Schmitz The patient had a small bowel series and barium enema in November 1958 The small bowel series was negative On the previous examination there was marked shortening of the colon and on this last examination in November of this year there has been improvement in the degree of contraction (Fig 3)

Dr Bargen I have often heard it said that the changes in the colon of this disease are irreversible I have long been convinced that that is not correct We have many films which show even a much greater change than here depicted The roentgenogram at times becomes quite normal after a period of treatment

Here we have a patient who was very ill and opinions differ as to whether she should have been operated or treated medically She made a nice symptomatic recovery and there has been some improvement in the bowel structure Now obviously there must be many other patients in whom this happens and the question of when surgery should or should not be done is often difficult to decide

I shall call now on Dr Schmitz to show us some films of some of the different features of ulcerative colitis and I would like to call on Dr Dragstedt further for some of his opinions about

fonamide intolerance to it I have no particular preference for it except that it seems to be tolerated well over a long period of time

Dr Elliott The use of Azulfidine® in our hands has worked very effectively I don t know why it works and I don t think most people do It has some antibiotic action and just recently we have gone into this very deeply to the point actually now of treating all of our people with Azulfidine® either combined with steroids or without, and in all types of cases On most cases we have kept them on the medication for prolonged periods and this ranges from six months to a year We have had very little side reactions to it it is an effective medicine We have generally kept them on maintenance dosage of 4 grams a day This may vary to as high as 8 grams or as low as 2 grams

Dr Bargen For what period of time do you use steroids?

Dr Elliott That will vary too considerably but we tend to use them much longer than we used to I think it has been the common experience of all internists to have these people get well rather quickly as far as appearance is concerned such as the patient we saw today but when you look at these people through a sigmoidoscope you may still see very active disease That is our indication to continue steroids On an average it has been running 8 12 months

Dr Bargen Do you have periods when you stop the hormone or do you give it continuously?

Dr Elliott We give it continuously and judge it almost entirely by our sigmoidoscopic picture

Dr Bargen In spite of the opinion of our surgical colleagues the patient s symptoms appear to be under control at this time Dr Elliott s discussion has been very much to the point However I give Azulfidine® in courses until the patient is asymptomatic I usually give patients a rest after a few weeks

Dr McHardy Our procedure is to give it as you do until we are assured that the process becomes quiescent then we give it at least one week out of every month for an indefinite period varying with the patient response We don t know exactly what

came in in 1956 and had what we thought was a negative colon examination However the patient went steadily downhill and on subsequent examination we saw marked changes of ulcerative colitis The changes that we generally see in early ulcerative colitis are an increase probably in the submucosa and mucosal tissue so we have a marked exaggeration of the folds A frequent finding in ulcerative colitis is the tiny mucosal ulcerations that penetrate and undermine the mucosa There are times when the ulcers get larger and go through the submucosa and later the undermined areas may become confluent over a certain segment of bowel It is rather difficult to demonstrate thickening of the bowel wall because in most cases we see only the mucosal surface of the bowel wall and not the outer surface However in the rectum by looking at the border between the rectum and the sacrum with lateral projection we have some idea how thick the bowel wall is although the amount of fatty tissue here varies from person to person

Another change that we see quite commonly in ulcerative colitis are pseudopolypoid changes and these of course are just the hypertrophied remnants of the mucosa These have a rather characteristic appearance and it is interesting to note that we can have very severe pseudopolypoid changes without noticeable contraction or shortening of the bowel itself In this next case the curvature is fairly normal although we have extensive changes in the mucosa and then as the disease progresses we have the changes of a more marked nature where we start to get a shortening of the bowel and the mucosa becomes rather atrophic and the colon becomes extremely rigid marked shortening of the colon follows You notice that in destruction due to the granulomas such as regional enteritis the bowel wall is not very thick although it is a little thicker than normal Ulcerative colitis is a pleomorphic disease and the changes depend on the stage of the disease

Dr Bargen In an hour and a quarter we can only touch on the high points of a disease of this kind

Dr Dragstedt when do you operate on these people? What are the indications for surgery?

Dr Dragstedt The result of medical treatment in this patient



Figure 3

surgery and perhaps he will show us some films of the ileac stoma that he has designed

Dr McHardy In the interval Dr Bargen would you give your opinions on Truelove's method of rectal treatment with steroids?

Dr Bargen I shall get to that after a while

Dr Schmitz I think it is not too uncommon to have a patient with a clinical picture of ulcerative colitis with a normal barium enema This is easily understood The x ray demonstrates gross pathological changes and if all that is present is an early mucosal change we will not demonstrate the disease This patient



Figure 4

surgical treatment There is a further large group of patients who are not doing very well on medical treatment This case today was a very nice case to select and I am sure Dr Dragstedt will agree with me I wish we didn t have to operate on any of them and I am sure that he feels the same way There are patients with acute ulcerative colitis who do not respond to conservative treatment The mortality rate is very high in this disease and in such patients we should be inclined after reasonable trial of two to three weeks of medical treatment to

has been very good surprisingly good I would not have anticipated this degree of reversibility in a colon involved to this extent I must admit that what the surgeon has to offer a patient with chronic ulcerative colitis is not very good We can remove the colon and prevent further progress of the disease Thus on the positive side we remove the possibility of subsequent formation of carcinoma in the diseased colon On the negative side we give the patient a permanent ileostomy This is disagreeable and is subject to dysfunction There is also an appreciable mortality associated with the operation itself Dysfunction of the ileostomy can be ameliorated by skin grafting the protruding segment I introduced this method of operation several years ago and have found it to be quite satisfactory in preventing excoriation of the skin and prolapse (Fig 4)

Dr Bargen I would like to substantiate Dr Dragstedt s comments by saying that his is the most satisfactory ileac stoma that I have ever seen I am fairly familiar with the Turnbull Brooka and other types of mucosal grafts but I have seen less trouble with this than with any other type of ileac stoma

Dr Goldman will you cite your indications for surgery?

Dr Goldman I think that the complications of this disease are indications for surgery Certainly the patient who has a perforation of the colon from an ulcerated or necrotic area or a patient who has a perforation with an abscess has an indication for surgery Other indications are in the patient who has a severe continuing hemorrhage from the colon which occurs in a small per cent patients who have an obstruction of the colon from cicatricial contracture as a result of healing in a previously inflamed part of the colon also the patient with the possibility of malignancy for as Dr Dragstedt said this type of malignancy in the colon is usually fatal Then there is another group of patients who have what we might call impending perforation These patients have the development of abdominal pain some distention and the x ray film shows a large dilated colon This has been written about and is termed acute colonic dilatation meaning that the inflammatory reaction is so marked that perforation is imminent so that in such patients one might consider

the mortality rate will be high it used to be about 50% just for the ileostomy Now the mortality rate is very low if we also remove the colon In these patients we usually put them on cortisone before surgery and many of them who are in very poor condition temporarily improve after a few days of cortisone therapy so that we can go ahead and operate

Dr Bargen What do you think about the recent British opinion of doing an ileorectostomy in these cases?

Dr Dragstedt Removal of the colon with anastomosis of the ileum to the rectum in patients with chronic ulcerative colitis is not a new operation I had an unsatisfactory experience with it many years ago The rectum remained diseased and continued to discharge blood and pus for years Also I had one patient who developed a carcinoma in the retained rectum from which she died. I fear that it is not a good procedure but my mind is open

Dr Bargen We gave up the procedure of ileorectostomy 20 years ago During my years of managing patients with this disease we have gone through periods of surgical trends In the early days cecostomy was an accepted procedure then appendicostomy then ileostomy colostomy and finally colectomy Most patients with ileorectostomy find it necessary to wear a diaper Some of these patients have 15 and more stools a day and are very unhappy

Dr Elliott how long do you use ACTH I V in a fulminating case of ulcerative colitis before surgical intervention?

Dr Elliott Not too long I would say not more than three to four days at the most and seldom that long I V ACTH is a very effective way of giving steroids to an acutely ill individual It can be dangerous and it has the particular danger of masking some of the more ominous signs as Dr Goldman has mentioned particularly impending perforation Unless we have reasonable evidence to show that this patient is steadily improving I would hesitate to continue ACTH or indeed any type of medical therapy beyond five days particularly in an acute case of colitis gravis

Dr McHardy what do you think?

Dr McHardy I am a little hesitant in my answer I think

operate These people are very ill have a high fever rapid pulse some of them have chills They lose weight rapidly and many of them lose fluid by emesis and diarrhea We occasionally operate on them and the result is quite good even though the patient s condition is very poor It is still very difficult to evaluate conservative therapy in this disease since sometimes there is a coincidental relationship between the administration of the drug and the remission that the patient had This patient that we saw today still has a very badly diseased colon and she can still develop any of these complications The incidence of malignancy in early cases doesn t concern us too much but in those cases that go along eight to ten years or more there is a significant incidence of malignancy if their disease is still present This incidence is reported as high as 10% for 10 years and 20% for 20 years If the occurrence of malignancy is coincident with fatality it should cause us to consider operating on patients who have gone for many years and who still have a diseased colon so that in all of those instances I think that we have to consider surgical treatment if the indications are present

Dr Bargen In line with what you and Dr Dragstedt have just said I would like to ask you would you do a total colectomy or just an end ileostomy in a fulminating case of ulcerative colitis not responding to medical therapy?

Dr Dragstedt I think I would do a total colectomy by the two team technique I would prepare the patient by blood and plasma transfusions and then go ahead I would remove the colon and rectum in one operation There are some cases however where I would consider a preliminary ileostomy to divert the fecal current and then at a later stage remove the colon and rectum An ileostomy is not apt to be adequate in such a *fulminating case and I would go ahead with a total colectomy*

Dr Bargen Do you agree with that Dr Goldman?

Dr Goldman Yes I think that this is a different situation than Dr Dragstedt talked about before when he talked about the excellent results that some patients will get with just an ileostomy When acute ulcerative colitis is present if we do not remove the focus of their sepsis at the same time as we do the ileostomy

be used and transfusions, if necessary If the patient does not respond to this regimen then I would be inclined to add steroids to this therapy not I V but by mouth

Dr Bargen Now Dr Elliott could you tell us a little more about the use of steroids in these cases?

Dr Elliott We have been using mostly the suppositories of one form or another for the last several years mainly in patients with early proctosigmoiditis Recently we have devised a method of administering this by proctolysis similar to Truelove s work in England We ve been using Medrol® 40 mg per cc and we have been using 40 mg per dose with 4 6 oz of tap water We have the patients mix it and administer it by proctoclysis and they retain it until the next morning Now this is somewhat of a burden and somewhat of a chore for these individuals but it is a very effective way of going about things particularly in the early acute case There is no question that these drugs are topically effective and we ve been able to quiet down some of these patients very well Now I don t know what is going to happen to them Several of these individuals symptoms disappeared and haven t returned The longest period of follow up was eight months But it is an effective way of going about this particular type of case

Dr Bargen How soon do you get results?

Dr Elliott We have seen significant results with the sigmoidoscope within 36-48 hours

Dr Bargen I think that has been the experience of others It must be said however that before we had these newer agents these patients became asymptomatic It took a longer time This seems to be an adjunct in helping a number of these patients to make a quicker symptomatic recovery I am not sure this justifies the use of steroids in this manner

Here is a question from the floor I would like to know what the opinion of other members of the Panel is regarding the question "Is not ulcerative colitis a contraindication to pregnancy?" You heard Dr McHardy s comment I would like to hear the opinion of the others Dr Elliott

Dr Elliott No I don t think it is a contraindication And

we have been guilty of treating patients longer than that and have had the good fortune of having some of them eventually respond In some instances it is probably accidental or providential that they did recover We have continued to treat patients for longer periods of time in some instances because the patient has refused surgery and we have thereby achieved unexpected responses The longest period of therapy I can recall was 14 days We have felt very much as Dr Elliott if the patient is not responding after a period of five to seven days more prolonged therapy is unlikely to prove encouraging There are, however other circumstances which change one s decisions at times There is one little difference of opinion however I feel that Dr Goldman was describing somewhat the same situation to which Harry Bockus has given the name— toxic aganglionic megacolon referring to these impending perforation patients The patient has a tremendously dilated colon we have seen some patients develop this while on ACTH We have had three cases operated with three fatalities The more recent cases therefore have escaped surgery and survived We are actually afraid of these patients as surgical risks

Dr Bargen We have had the same experience

We have spoken a great deal about the patients with the fulminating disease Lets turn for a moment to the patients with mild disease who I am sure no one on this Panel would wish to treat surgically I am referring to those patients who have the proctoscopic and sigmoidoscopic picture of the disease only How do you treat these Dr Hand?

Dr Hand I would treat these as we used to treat them before we had the steroids By that I mean general supportive measures using everything we can use to support the patient such as diet supplemental vitamins blood transfusions and Azulfidine® etc It now appears that Azulfidine® is superior to Sulfathalidine® and sulfadiazine in ulcerative colitis I would use a bland diet but I would try to get as much protein into the patient as possible If his history or response suggests he may be allergic to milk I would try to eliminate milk as much as possible during at least the acute phase of the disease Also some type of iron should

be used and transfusions if necessary If the patient does not respond to this regimen then I would be inclined to add steroids to this therapy not I V but by mouth

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incidentally we have carried two women in this institution through a pregnancy on continuous steroid therapy without any aggravation who had pre existing severe and pronounced disease in the bowel Although pregnancy has an occasional tendency to aggravate the disease there are so many factors of emotional components in one s approach toward the pregnancy that no hard and fast rules can be laid down I have never seen the case yet, where I felt a therapeutic abortion was indicated

Dr Bargen I agree with that Here is another question "Is steroid therapy continued throughout pregnancy if the sigmoido scopic examination shows active disease?

Dr Hand would you comment on this?

Dr Hand I think Dr Elliott just answered that

Dr Elliott We have continued some patients on steroids throughout pregnancy

Dr Bargen A great many other questions have been sub mitted but it would be impossible to cover them even before 7 o clock I would like to address this to Dr McHardy Do you think the result with the patient you just saw would have been achieved if milk had not been eliminated?

Dr McHardy I think there are some patients who are intol erant to milk because of diarrhea In such patients I feel that it is certainly considered contraindicated We as a policy do not give milk to our patients with ulcerative colitis We have found that it does have a diarrheal tendency We do not feel that it is etiological in any way but it irritates and causes more difficulty

Dr Bargen We come to one question which of course should have had more time What is the Panel s opinion about the use of psychotherapy in ulcerative colitis

How many of your patients Dr Hand do you send to the psychiatrist?

Dr Hand None

Dr McHardy None for the treatment of ulcerative colitis

Dr Elliott Same as Dr McHardy

Dr Bargen I think that points up the problem in dealing with such a severe disease Surely there are cases where a psychiatrist could be of help The patient s emotional side may be an impor

tant factor while not in the inception of the disease at least in its relapses

Is the incidence of carcinoma in this disease related to the amount of activity of ulcerative colitis? Would a patient with intermittent disease be as prone to carcinoma as one who has it all the time?

Dr Dragstedt I couldn t answer that

Dr Bargen I don t want you to leave here with the idea that 30-35% of patients with ulcerative colitis develop carcinoma The longer these patients go with recurrent attacks the more likely they *are to develop carcinoma but the incidence is still very* small

You have all seen a patient this afternoon who was very sick, who did make a recovery and apparently the disease is reversible Certain indications for surgery have been expressed Opinions when patients should not be operated have also been heard Something has been said about steroids and when they should not be used and the value of Azulfidine® has been extolled We have also learned that some of these patients are sensitive or allergic to some foods I hope the expressions by the panel will help you in your daily management of these patients

NEWER DRUGS
IN THE THERAPY OF CONSTIPATION

FREDERICK STEIGMANN M S M D *

BEFORE discussing the topic of newer drugs in the treatment of constipation let us first define the subject of constipation and the indications for drug therapy

Constipation is the most common of all disorders of the digestive tract Some have termed it as the most common complaint to which the human race is heir others as the greatest single medical problem of the American public after the age of forty If Hurst s definition of constipation as A condition in which none of the residue of a meal taken eight hours after defecation is excreted within forty hours is accepted the next step should be to determine whether the failure of excretion is due to an organic obstacle which can only be remedied by a surgical procedure or whether it is due to a functional cause and hence must be treated with all and varied means on hand

Functional constipation represents three main types which must be elicited from the patient by a careful history To some patients constipation represents insufficient frequency of defecation that is once in three four or more days To others it represents an insufficient quantity of stool even though there is a daily bowel movement To still others constipation means abnormally hard and dry stools (Table I)

* Associate Professor of Medicine University of Illinois College of Medicine Chicago

TABLE I

DEFINITION AND CLASSIFICATION OF FUNCTIONAL CONSTIPATION

FUNCTIONAL CONSTIPATION

A Condition in Which None of the Residue of a Meal Taken 8 Hours After Defecation is Excreted Within 40 Hours (Hurst)

TYPES OF CONSTIPATION

1 Insufficient frequency of defecation
2 Insufficient quantity of stool
3 Abnormally hard and dry stools

CLASSIFICATION

1 *Colic Constipation—delayed passage through colon—defecation normal*
2. Dyschezia—no delay in passage but evacuation is delayed
3 Constipation—due to insufficient feces

For the practicing clinician constipation may be classified into three groups

1 *Colic constipation* that is constipation caused by a delayed passage of the stool through the colon but once the stool has reached the rectum defecation occurs normally

2 *Dyschezia*—a type of constipation in which the passage through the colon is normal but the evacuation of the stool from the rectum is abnormally long delayed

3 *Constipation due to insufficient feces* This type of constipation is mainly on the basis of insufficient roughage material being present in the gut

It is not within the scope of this paper to go into great lengths regarding the many possible etiologic factors of constipation A few main causes however must be mentioned inasmuch as the drug therapy may have to be given accordingly The causes of colic constipation may accordingly be subdivided into those due to (A) deficient motor activity of the colon (B) diminished reflex activity (C) inhibition of motor activity and (D) lack of excessive force needed to carry the feces through the intestine

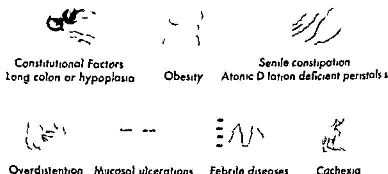
Deficient motor activity is commonly the result of weakness of the intestinal musculature and may be due to a variety of factors Some of these may be constitutional like a hypoplastic musculature of the colon or due to changes brought on by aging that is atonic dilatation with resultant deficient peristalsis Weakness of the intestinal musculature may be also brought on by cachexia

febrile diseases mucosal ulceration obesity and chronic overdistension of the intestinal wall (Table II)

Diminished reflex activity is the result of insufficient stimulation

TABLE II

CAUSES OF COLIC CONSTIPATION DEFICIENT MOTOR ACTIVITY—WEAKNESS OF MUSCULATURE



of the neuro muscular apparatus This may be caused by a deficient gastro colic reflex or deficient peripheral reflex It may also be the result of deficient secretion of the ductless glands or of deficient excitability of the intestinal mucosa or by a depression of the nervous system (Table III)

TABLE III

CAUSES OF COLIC CONSTIPATION DIMINISHED REFLEX ACTIVITY

A Insufficient stimulation due to
  1 Deficient gastro-colic reflex
  2 Deficient peripheral reflex
  3 Deficient secretion of ductless gland
  4 Deficient exercise
B Deficient excitability of intestinal mucosa
C Depression of nervous system

Inhibition of motor activity of the intestine is usually the result of (1) direct stimulation of the inhibitory fibers (2) reflex inhibition of intestinal activity or (3) psychic depression (Table IV)

TABLE IV

CAUSES OF COLIC CONSTIPATION INHIBITION OF MOTOR ACTIVITY OF THE INTESTINE

A Direct stimulation of the inhibitory fibers
B Psychic depression
C Reflex inhibition of intestinal activity

In some patients colic constipation results from the lack of the extra force necessary to carry feces through the intestine Such an extra force is usually needed when the feces are excessive or when there are partial obstructions along the gastrointestinal tract as from gummy substances or fecal concretions or if the feces are too dry because of (1) not sufficient water intake (2) excessive water loss, or (3) excessive absorption of water from the colon (Table V)

In evaluating which of the variable causes may play a causative role in the constipation of the presenting patient one must consider the possibility of the patient's ingestion of any one of the many presently used drugs which are conducive to constipation Among the most recent ones the hypotensives tranquillizers and anticholinergics are the greatest offenders

TABLE V

CAUSES OF COLIC CONSTIPATION EXCESSIVE FORCE REQUIRED TO CARRY FECES INTO SMALL INTESTINE

A Feces are excessive

B Feces too dry



Not enough water intake

Excessive loss of water

Excessive absorption of water

C. Obstruction along G I tract



Obstructions along G I tract
e g gummy substances, fecal concretions

Dyschezia is usually the result of (1) inefficient defecation and (2) obstacles to efficient defecation. Rarely it is on a purely hysterical basis.

Inefficient defecation is usually caused by habitual disregard to the call of nature or to suitable posture. Occasionally weakness of the defecation reflex is the cause.

Obstacles to efficient defecation consist mainly of abnormally hard and bulky feces and of functional and organic obstructions in the rectal area like spasms from and irritation and pressure from neighboring pelvic organs (Table VI).

TABLE VI
CAUSES OF DYSCHEZIA

I INEFFICIENT DEFECATION

A. Habitual disregard to call of nature



B Unsuitable position



C Weakness of defecation reflex

II HYSTERICAL DYSCHEZIA

III OBSTACLES TO EFFICIENT DEFECATION

A Abnormally hard and bulky feces





B Functional and organic obstructions.

Finally some patients suffer from constipation which is mainly due to (1) insufficient food residue reaching the rectum because of a small quantity of ingested food and (2) little material reaching the rectum because the food eaten is so bland that it is completely digested (Table VII).

TABLE VII
OTHER CAUSES OF CONSTIPATION

CONSTIPATION DUE TO QUANTITY OF FECES BEING DEFICIENT

I Insufficient food residue reaching the colon

II Food ingested is completely digested only little material reaches the rectum (greedy colon)

In some instances the patient s history and findings may suggest a combination of some of the factors discussed above rather than any of them alone Thus a patient may be constipated because of poor bowel habits improper diet insufficient fluid intake excessive nervous tension painful defecation from a tight sphicter anal fissure etc or an atonic musculature (old age) in addition to some other disturbances that is hypothyroidism deficient bile gastric or pancreatic secretion or due to the ingestion of various costivogenic drugs or irritating laxatives

Having obtained some evaluation of the possible cause for the existing constipation in a particular patient, the next step is to eliminate by appropriate laboratory and other special examinations any organic cause For this complete x ray studies of the gastrointestinal tract proctoscopy as well as different chemical serological and endocrine studies may be necessary The ultimate diagnosis of functional constipation can only then be confirmed if the complete workup fails to reveal any organic pathology

The diagnosis of functional constipation will suggest to the clinician first a hygienic regimen (Table VIII) which will do away with some of the conducive causes and which will train the patient how to live correctly so as not to become constipated Secondly a dietary regimen will have to be prescribed for the patient which should prevent causative factors and institute helpful diets for prevention of constipation (Table IX) Finally the need for drugs will have to be carefully evaluated concerning the type quantity and mode of administration In other words the patient with functional constipation requires a prolonged coordinated attack on his condition before any noticeable steady improvement will be noted

Despite the fact that constipation has been termed the most common complaint to which the human race is heir too frequently it is given less attention by some clinicians than is given to comedones in a teenager Not only do some clinicians completely ignore the complaint of constipation but they even dogmatically state that there is no need for medication to relieve it In other words since it is non existent it needs not to be treated It is therefore noteworthy that a great clinician like A

TABLE VIII

HYGIENIC PROCEDURES IN THE TREATMENT OF CONSTIPATION


Squatting position


Commode for bedridden patients


Low seats for children—no dangling of feet


Sufficient time in comfortable place


Regular time daily—best after breakfast


Obey call of nature at any time


Eradicate fixed ideas about constipation—faddists for food or medication


Erase doubts of a must daily BM and of a must certain quantity


Erase doubt about normalcy of GI tract by complete GI X-ray


Relieve visceroptosis


Hydrotherapy cold stimulates musculature


Massage and exercise

Hurst presented his opinion of this matter in the following comment

Although the indiscriminate use of purgatives may have serious results their dangers have been exaggerated by some authorities who recommended that drugs should only be given as a last

TABLE IX

DIETARY PROCEDURES IN THE THERAPY OF CONSTIPATION



Frequent feeding.



Use with all meals.
Vegetables and fr its to g much cell lose organic acids, s ga and alkal salts.



Suitable d et of sufficient food



Take sufficient fl id —water sou m lk, ider beer—No strong tea



Oatmeal ce eals, should be av ded by sufferers from hemor ho ds)

E t slowly mastic te w ll (Att on to teeth)



I crease amount of fat b tte o l cream, bacon.

— —

recourse when all other methods have failed It is indeed doubtful whether more harm does not result especially in children from the excessively irritating diet sometimes recommended than from properly regulated doses of aperients

Our group has been in complete agreement with the above and we have treated our patients with functional constipation along the lines presented namely we have combined the hygienic dietetic and drug regimen for as long as the patient needed it It has been found that as soon as the patient will do well on the hygienic and dietetic regimen he will automatically decrease and finally completely stop the ingestion of any laxative

The wide use of over the counter laxatives or cathartics is the result of first a popular idea—in most instances correct—that for constipation as diagnosed by the particular individual the same family household remedy used by previous generations will help in his case too Secondly the lack of interest by some doctors in even discussing the matter of constipation with the patient but just telling him get "this or that" again compels the patient to buy his laxative over the counter Not until the doctors—like some

gastroenterologists do at present—will investigate each patient who complains of constipation according to the above outline will they be able to control the drugs used for the treatment of constipation

Without being too critical it might be stated that not only do patients follow a certain pattern in the choice of their favorite medications for relief of constipation but some doctors also seem to have their favorite few which they might have inherited from their preceptor or obtained from their favorite or vociferous "de tail man In justice to many of our practicing colleagues it must be mentioned that it is impossible for some of them to keep up with the flood of new drugs that are weekly or monthly thrust upon them and that they will therefore stick to some of the old time honored and proven ones rather than embark on new "un charted seas Nevertheless one must admit that some of the newer products do frequently possess desirable attributes and should therefore be preferred to the older ones even though the latter performed well in their time

Some of the drugs which have been used in the treatment of constipation can be listed briefly as falling into the following groups

1 Hormones e g thyroid
2 Alkaloids e g nux vomica
3 Synthesized laxatives e g phenolphthalein
4 Bulk increasers e g
   Agar agar
   Psyllium
   Methylcellulose
   Guar etc
5 Saline laxatives e g Magnesium Sulfate
6 Mercurials e g Calomel
7 Lubricants e g Liquid paraffin
8 Vegetable stimulant laxatives e g
   a Castor Oil
   b Anthracene Compounds e g
      I Aloes
      II Cascara sagrada
      III Senna

Of these some like the mercurials have completely gone out of use others like alkaloids and hormones are mainly considered as secondary adjuvants and still others like the saline laxatives have become indicated only under special circumstances Only the bulk increasers the lubricants and the vegetable stimulant laxa tives have persisted because some of them in particular have been changed and improved to meet the present demand

Among the newer drugs in the treatment of constipation one finds therefore a number of substances belonging to the above latter three groups plus some additional ones the action of which is based on entirely new concepts

In the *Physicians Desk Reference* 1958 a total of 115 substances are listed as laxatives In the Modern Drug Encyclopedia and Therapeutic Index of 1958 sixty-one substances are listed under laxatives In this issue moreover the term fecal softeners" appears for the first time listing thirteen such substances To demonstrate the "fertility" of the manufacturers of laxative substances one can refer to the Third Edition of the *Medical Drug Encyclopedia and Therapeutic Index* of 1947 which lists one hundred laxatives of which sixty eight are not found anymore in the Seventh Edition published ten years later (Tables X XI) The

TABLE X

LAXATIVES PUBLISHED IN MEDICAL DRUG ENCYCLOPEDIA 3RD EDITION 1946
BUT ABSENT FROM 7TH EDITION 1958

ALBA-CAR PREPARATIONS	CHOLAPHEN
ANALAX	CHOLO GLYCO WITH CATHARTICS
BARAVIT	CHOLPENOLATE
BARAVIT WITH CORTEX FRANGULA	FRANCALL
BETAJEL	GEOL
BETAKAR	GLYMOL
BETAPHOS	HEPATONE
BICAREX	I SO GEL
BICHOLATE	ISTIZEN
BILATICOL	KARABIM
BRENGAL	KASAGRA
B S P TABLETS	KAYLFNE
BUFFER PHOSPHATES	L A FORMULA
CAL-EXTRACT	LAPACTIC PILLS
CARICA BILE	LAXAMEL
CASTALOIDS	LAXATIVE TABLETS
CHIONIA	LIQUID ALBOLENE

Seventh Edition however contains thirty four substances which have not been present in the previous editions among them the thirteen substances listed as fecal softeners (Table XII) The great number of substances listed is in most instances not due to newer chemical compounds but to the tendency of mixing pre

TABLE XI

LAXATIVES PUBLISHED IN MEDICAL DRUG ENCYCLOPEDIA 3RD EDITION 1946 BUT NOT IN 7TH EDITION 1958 (CONT)

LORAGA	PURSIN LAXATIVE TABLETS
MAGOLEUM	SAGRADOL
MALTINE WITH CASCARA SAGRADA	SALITHIA
MAOLIN PREPARATIONS	SAL LAXA
MUCARA	SODOLATE
NEOLOID	SYL AG OL
NEO PROBILIN	TAM
NUCARPON	TAUROPHEN
NUCOLEX	THALOSEN
OCCY CRYSTINE	TOROCOL
OLGAR	UNI B I
OXOLAX	URIMENE
PEKTOZ	VERACOLATE
PERISTALTIN	VITAGA
PERTOMALT	VITAGAR
PHENOVAL	VITAPECTOSE WITH KARAYA
PULVERCIN	WYALIN

TABLE XII

LAXATIVES PUBLISHED IN MEDICAL DRUG ENCYCLOPEDIA 7TH EDITION 1958 BUT NOT IN 3RD EDITION 1946

AGAROL LIQUID	KONDRETABS TABLETS
ALOPHEN CAPSULES PILLS	MALT SOUP EXTRACT
AQUATYL TABULES	MILKINOL
BILINATES TABLETS	MODANE
CASYLLIUM	MUCARA
CELLOTHYL TABLETS	MUCILOSE
COLOGEL LIQUID	NEO CULTOL
COLOVAC TABLETS	PERI COLACE
DORBANE SUSP TABLETS	PETRONOL MINEROL OIL
DORBANTYL CAPSULES	PLANCELLO TABLETS
DOXINATE WITH DONTHRON CAPSULES	PRULOSE TABLETS
EMULSEROL CASCARA	SENOKOT WITH PSYLLIUM LIQUID
HYDROLOSE SYRUP	STUART C M C CAPSULES
IMBICOLL B_1 GRANULES	TURICUM LIQUID
ISOCRIN TABLETS	X PREP POWDER
KALPIN	ZYLAX TABLETS
KONDREMUL	ZYMELOSE GRANULES

viously known laxatives and marketing the mixture as a new laxative

It is obvious therefore that most of them have failed to prove

their efficacy and were therefore discarded It is also equally obvious that no doctor can familiarize himself with all of them but will either stick with the few he has known or perhaps add one or two new ones to his armamentarium I will therefore attempt here to discuss briefly the indications and advantages of a few of the newer drugs used in the treatment of constipation

In the last decade one of the oldest known laxative substances —Senna—was completely explored with the resulting development of a fully stable powdered senna preparation from the residual pericarp of the pod The preparation contains all desirable laxative components of the senna pod and is at the same time free of the impurities which in previous liquid preparations of senna were the cause for the griping and instability Clinical observations in England where the preparation was developed and observations in this country including our own have demonstrated the efficacy of this new senna powder in most patients with functional constipation The original pharmacologic studies on Senokot® in Europe suggested that the inactive glycosides are absorbed in the small intestine and are carried by the blood stream to the colon where by bacterial action they are changed into active aglycones The latter directly stimulate Auerbach's plexus thus stimulating a normal physiologic effect by initiating peristalsis of the colon without affecting the small bowel

In our studies covering approximately three years Senokot® has been found useful in pregnant women in constipated children and particularly in geriatric patients who need a stimulant laxative more than just a bulk producing substance Senokot® has also been of value in the constipation secondary to the use of ganglionic blocking agents tranquilizers and anti cholinergic substances Despite its sweet taste and granular appearance it could be used satisfactorily in cases with diabetes and peptic ulcer respectively Moreover unlike some other laxatives Senokot® can be given safely to women in the postpartum period because it is not excreted in the breast milk

The action of Senokot® has in recent years been enhanced in some patients by combining it with a stool softener This new mixture (Senokap®) permits first the hydration and softening of the stool so that the subsequent peristalsis initiated by the senna

powder will more readily move along the softened fecal mass This preparation is suited for patients who because of dietary–quantitative and/or qualitative–restrictions are bound to have only little bulk reaching the colon

A mixture of the stable senna powder and dehydrocholic acid has recently found good acceptance by patients who have chronic biliary complaints in addition to constipation

Since the appearance of Wilson s and Dickinson s report about the efficacy of dioctyl sodium sulfosuccinate for constipation this substance has been introduced singly or in combination with others under a variety of names for the treatment of constipation Its main action seems to be softening of the fecal mass within twenty four to forty eight hours In some patients this action alone seems to be sufficient to permit the atonic musculature to move the fecal mass in others a stimulant laxative is additionally needed (Senokap® Dorbantyl®) While it has been introduced originally as correcting constipation without the obstipation of bulk cathartics recently some manufacturers prepared mixtures containing dioctyl sodium sulfosuccinate as a wetting agent and carboxymethyl cellulose or similar substances as lubricating gels for the use in functional constipation

More recently a new substance Dulcolax® (brand of bisacodyl) was introduced the effect of which is due to direct action on the colonic mucosa whether taken orally or as suppository Personal experience with this preparaton has been too limited to express any definite opinion However it is contraindicated for use in patients receiving antacid therapy

Similarly personal experience with Pharmalax ® the new laxative suppository has been too limited It is supposed to work by releasing carbon dioxide in the colon and thereby bringing about complete evacuation within thirty minutes

SUMMARY

Chronic functional constipation continues to be one of the most common complaints of patients consulting a physician for gastrointestinal symptoms or symptoms of other organ systems Despite the frequency of these complaints many physicians are prone to ignore them or to give them only superficial heed As a result of

thus the patients become accustomed to treating themselves by using any laxative suggested to them by their family members friends and neighbors Frequently these persons use any or all of the laxatives highly advertised through various channels—radio television newspapers or magazines

It is our opinion that when a patient complains of constipation he should have a complete checkup to rule out any organic pathology Once this is eliminated and the particular type of functional constipation is determined the physician should prescribe for the patient a suitable dietary and hygienic regimen complemented by an indicated laxative The type of laxative and the length of time it should be taken will depend on the patient s general response to this management From the data presented it would appear that in most instances of functional constipation the best suitable laxative would be one which has a mild stimulant *effect on the colon without disturbing the activities of the* small bowel Preparations of the vegetable stimulant group of laxatives particularly of senna e g Senokot® seem to answer this demand The pure softeners may be of value especially in those few cases where hard stools are the main cause of the constipation *However a combination of a stimulant laxative with a fecal* softener e g as in Senokap® may be of more benefit to many patients than either alone The role of the most recently introduced substances which are claimed to stimulate the colonic mucosa directly needs more time for evaluation

powder will more readily move along the softened fecal mass This preparation is suited for patients who because of dietary–quantitative and/or qualitative–restrictions are bound to have only little bulk reaching the colon

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SUMMARY

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Dr Wilbur You already have heard something about functional constipation this morning Dr Steigmann emphasized the frequency of it I would say that constipation is the most common symptom of functional disturbance of the gastrointestinal tract I think Dr Steigmann did a good job this morning in defining constipation Each individual here and I am sure each adult in this country knows what constipation means It is one of those terms which may not be too easily defined scientifically However it is a term which everyone understands satisfactorily

One point along the line of the presentation that Dr Halpern made which was of some interest to me was the picture of the little house with the crescent on the door I was in Alaska some years ago and one of the interesting things pointed out by the physician who took care of the snow troops was that those men who were all day long and all night long in temperatures of 40 50 below zero had constipation as their most important medical problem I think you can realize why it was such a common one To try to relax a certain sphincter in temperatures of 40 50 below zero is not easy

This panel has presented some very interesting basic scientific discussions this morning Now we come down to the meat of it for physicians and that is the presentation of a case and the application of some of this material to the common problem of constipation An illustrative case will now be presented by Dr Lee

Dr Lee D B a 28 year old white woman separated from her husband first came to the University of California Medical Clinic three and one half years ago complaining of increasing constipation She stated that at the age of 7 years after eating apricots she had had an *episode of severe diarrhea which lasted 4 weeks* Since that time she had suffered from constipation and could not remember ever having had a bowel movement without the aid of laxatives The interval between bowel movements was usually 3 weeks but at times was as long as a month *Stools were described as hard* dry and small and streaks of red blood in the stools during the previous two years had been noted Before her first visit to the Clinic she had been taking one-half to 1 cup of mineral oil once a week or 4 tablespoons of milk of magnesia twice daily

SYMPOSIUM ON FUNCTIONAL CONSTIPATION

Moderator

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Panel Members

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WALTER C. ALVAREZ, M.D., Emeritus Professor of Medicine, Mayo Foundation

ALFRED HALPERN, PH.D., Director, Department of Experimental Therapy, Stuyvesant Polyclinic, New York City

ROGER G. SIMPSON, M.D., Associate Clinical Professor of Medicine, University of California School of Medicine, San Francisco

FREDERICK STEIGMANN, M.D., Associate Professor of Medicine, University of Illinois College of Medicine; Chief of Gastroenterology Service, Cook County Hospital, Chicago

FREDERICK E. TEMPLETON, M.D., Clinical Professor of Radiology, University of Washington School of Medicine, Seattle

Case Presentation

JENNIE LEE, M.D., Fellow in Gastroenterology, University of California School of Medicine, San Francisco

A complete physical examination was done on March 21 1955 The pulse was 72 full and regular Blood pressure was 105/88 Examination of the head revealed it to be normal Examination of the eyes revealed the pupils to be regular and round. Extra ocular movements were normal The neck was normal Breasts were normal The lungs were clear to auscultation and percussion The heart was not enlarged and there were no thrills or murmurs Examination of the abdomen revealed no masses or tenderness The liver kidneys and spleen were not palpable The extremities were normal The rectal and pelvic examination revealed nothing unusual

Laboratory studies Routine blood counts were normal Urinalysis indicated no pathological condition Basal metabolism rate was plus 19 The protein bound iodine was 6 1 micrograms per cent Gastric analysis showed a maximum of 8 units of free hydrochloric acid in the basal fasting specimens

X rays The upper gastrointestinal tract series of films indicated no abnormality (*Figures I and II*) and no abnormalities were detected in viewing the barium enema films It was noted however that there was generalized slow filling of the colon

Proctoscopy Small internal hemorrhoids Findings otherwise normal up to 14 cm

Medical course The patient has been seen at fairly regular intervals in the Gastrointestinal Clinic for the past three and one half years She has been treated unsuccessfully with several laxatives and antispasmodics including phenobarbital and belladonna reserpine Mucilose® magnesium carbonate and Doxol® When she was first given magnesium carbonate it did not relieve her of constipation However in the year since separation from her husband she has been less nervous and upset and has recently found that after taking magnesium carbonate she has a liquid stool in the morning and 2 other liquid stools during the day She takes 4 tablespoonsful in hot water each evening at bed time She has found that it is not effective when taken in cold water She has discontinued the magnesium carbonate for as long as two weeks at a time but without it constipation nausea and retching always return

Dr Wilbur You can see that this patient has a very simple

When constipated the patient has always suffered from cramps in the lower abdomen and stinging pains in the rectum Constipation is also associated with severe headaches dryness of the mouth pains in the shoulders and the back of the legs severe nausea retching dizziness and a faint feeling

In childhood the patient had been taken to several doctors for treatment because of the constipation Treatments included the prescription of senna cascara mineral oil and milk of magnesia In 1954 she was hospitalized in Long Beach California because of constipation Barium enema x rays were taken and she was told she had a spastic colon During hospitalization she was found to be anemic and received one blood transfusion She was also dehydrated because of repeated vomiting and was given fluids intravenously for ten days

The patient s appetite has been good and she eats a regular diet She has tried eating large amounts of fruits and vegetables but found they have no effect on the constipation

Past history The patient has suffered no serious illness When she was a child tonsillectomy and adenoidectomy were performed

Family history Her father has asthma and a peptic ulcer Her mother suffered from constipation until she was about 40 years of age One aunt also suffered from constipation The patient has four brothers one brother has a peptic ulcer and the others are well She has four sisters one of whom has asthma and another constipation

Marital history The patient was married at the age of 21 and separated from her husband at the age of 27 She has had no pregnancies Her husband was studying to become a minister and did not want children until his studies were completed There was sexual incompatability because he did not feel it was right to have sexual relations unless they were going to have children The incompatability made the patient nervous and her constipation became worse

Systemic review Neurological review The patient had convulsions and frequent fainting spells in 1948 which were thought to be caused by thyroid insufficiency She took thyroid medication for one year

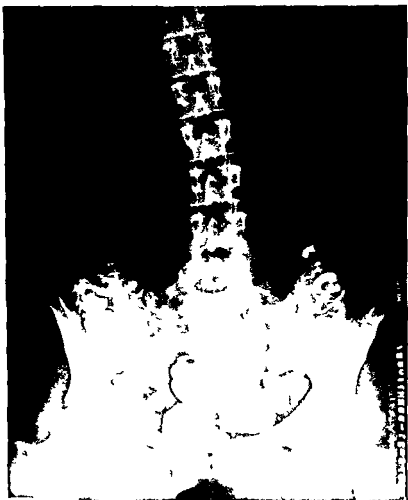


Fig 2 Evacuation view of colon

Dr Wilbur Do you happen to know if you were constipated before the age of seven?

Patient No

Dr Wilbur You do know that since then you have

Patient Yes

Dr Wilbur In the last month how have your bowels been?



Fig 1 Barium filled colon

history At the age of 7 following an episode of four weeks of diarrhea constipation began and has persisted

It lessened following her marriage eased up to some extent following her divorce It has led to all sorts of medical treatment most of which has been unsatisfactory One will have to say that this patient has constipation which is more severe than one ordinarily encounters

Patient Yes I remember once I didn t get rid of it for a couple of days They gave me medicine

Dr Wilbur I thought it might be of interest to ask each member of the panel to discuss some particular phase of the problem of functional constipation and to ask questions of one another to bring out certain points

One of the first questions I want to ask Dr Simpson and then discuss briefly is if there is any more information about the patient that he would like to have

Dr Simpson Why did they transfuse this girl in the hospital? What brought on such anemia that they decided to transfuse her? I would like to know what that point is

Dr Wilbur The reason for the transfusion is not known

Dr Simpson There is another thing that I would like to know There is reported a slow filling of the colon during the barium enema study Is there some organic reason for the delay? I doubt it but it is a thing I would like to know before I make a final diagnosis in this sort of case

Dr Templeton Was her colon clean at the time of the barium enema or was it filled with residual barium from the upper gastrointestinal study? We usually examine the stomach before the colon

Dr Rider Our routine here is just the opposite The colon first and then the stomach

Dr Wilbur While Dr Templeton is on that subject we might ask him whether as a radiologist he is satisfied that he has as much information as a radiologist can give that the barium enema is normal and the upper G I series is normal

Dr Templeton As a radiologist the primary function is to rule out an organic lesion such as a carcinoma some form of obstruction or *inflammation such as ulcerative colitis regional ileitis or* diverticulitis When we have done that we feel our job is done In this instance we might be able to tell something about the function of the colon We cannot go too far because we are examining the colon in an unphysiologic state An enema is not physiological *The colon must be clean in order to identify many* organic lesions Drastic catharsis is also necessary As a result

Patient I have to take medicine all the time

Dr Wilbur You have gone as long as a month without a movement?

Patient Yes

Dr Wilbur How often have you done that?

Patient Three different times I was in the hospital because it was a month

Dr Wilbur When you finally had a movement what sort of movement did you have?

Patient It was generally due to medication and I had quite a large one

Dr Wilbur Liquid?

Patient Usually liquid

Dr Wilbur Do you take an enema?

Patient I cant It wont go in I have had nurses try to give it to me and it just comes out

Dr Wilbur Will you tell us what you ate yesterday all day long?

Patient Eggs bacon toast soup sandwich salad turkey and dressing

Dr Wilbur Is there anyone in your family who is nervous?

Patient My father has an ulcer

Dr Wilbur Nobody had a nervous breakdown?

Patient No

Dr Wilbur Nobody has had falling spells?

Patient No

Dr Wilbur Do you get convulsions or do you just fall?

Patient Sometimes I just fall on the floor but no convulsions Usually it was just blacking out and having to sit down quickly

Dr Wilbur Did you ever hurt yourself falling?

Patient *Some bruises*

Dr Wilbur When you had these x ray examinations did the examination reproduce the cramp like pain that you have been having?

Patient I dont know

Dr Wilbur Do you have trouble getting rid of the barium that is used?

there and getting an outline of the colon In this sort of case it is fairly logical because we are not looking for tumorous lesion

Dr Templeton I am rather surprised to hear that this procedure is still done in a patient in whom there is no obstruction If the cathartic has not worked and there is fecal material it is not a good plan to try the barium enema The reason the cathartic did not work may be because of an obstruction low down When *obstruction is not present the fecal material is forced against* the cecum This sometimes causes the patient tremendous distress Then too a lot of fecal material is forced back into the terminal ileum I dont think that is good procedure

Dr Wilbur The 24 hour examination is worthless in 99% of patients and doesnt really give any useful information There isnt a thing demonstrated in a 24 hour examination that has not been demonstrated by a barium enema Without exception in the interest of studying a patient like this who has a constipation of unusual degree a 24 hour examination is a waste of time and a waste of money and as you can readily see from my comments I have no use for it

Dr Templeton May I mention the waste of money? In this day we must be very careful about the expense we add by keeping a patient in the hospital for extra examinations The worry about expense and the ill effects on the bowel caused by worry will offset the information obtained from the 24 hour colon examination

Dr Wilbur Perhaps I might also add—a little extra radiation I would like to ask Dr Albronda if he would discuss the psychodynamics of constipation as he feels they apply to this case

Dr Albronda You might remember that in my previous presentation I mentioned points in the history which should alert to the possibility that psychological factors are of prime importance in the genesis of the patients symptoms These points are Shifting complaints a *family history of emotional instability* evidence of nervous tension in childhood poor school and vocational record long medical history which includes often numerous operations many contacts with *physicians* disturbances in sexual relationships and current signs of nervous tension with or without the presence of significant organic disease

the colon may be fairly well irritated The various physiological changes *seen at fluoroscopy may not be identical to those that* usually occur in the patient

Dr Wilbur Years ago it was very common for radiologists to do and I understand sometimes they still do a 24 hour study after an upper G I series How much advantage do you think it is to you to be able to report to a physician that 24 hours after ingestion of barium that it has progressed to a certain point Do you think the information that you can gain is useful?

Dr Templeton I may be wrong in the eyes of some clinicians but it doesn t help me any Since psychologic factors have so much to do with the G I tract in an individual patient a 24 hour study does not aid very much

Dr Wilbur May I ask if any of the other clinicians here at the table feel that the 24 hour examination is of any practical value?

Dr Alvarez In a case like this I imagine it would be I would be interested in it

Dr Simpson I don t generally pay much attention to it It doesn t mean much In the upper G I tract it means a lot as far as gastric residue but in the colon it doesn t mean very much

Dr Steigmann I might say that in some of our studies attempting to prove whether a patient is constipated or just imagining things we followed the progress of the barium not just for 24 hours but until the bowel was completely empty We have had patients in whom it took 96–120 hours before the barium reached the colon and rectum and then it would stay there for another 48 hours Therefore in any patient in whom we are really interested to check bowel stasis it may be necessary to follow the barium meal every 24 hours for several days to see it leaves the rectum

Dr Templeton Actually we can get some information about how the colon functions by just taking a plain view of the abdomen You do get some information that way without giving a barium enema at all

Dr Simpson Some radiologists have advocated doing barium enema with no preparation at all with no cathartics no enema but just running the barium around whatever fecal mass is

there and getting an outline of the colon In this sort of case it is fairly logical because we are not looking for tumorous lesion

Dr Templeton I am rather surprised to hear that this procedure is still done in a patient in whom there is no obstruction If the cathartic has not worked and there is fecal material it is not a good plan to try the barium enema The reason the cathartic did not work may be because of an obstruction low down When obstruction is not present the fecal material is forced against the cecum This sometimes causes the patient tremendous distress Then too a lot of fecal material is forced back into the terminal ileum I don t think that is good procedure

Dr Wilbur The 24 hour examination is worthless in 99% of patients and doesn t really give any useful information There isn t a thing demonstrated in a 24 hour examination that has not been demonstrated by a barium enema Without exception in the interest of studying a patient like this who has a constipation of unusual degree a 24 hour examination is a waste of time and a waste of money and as you can readily see from my comments I have no use for it

Dr Templeton May I mention the waste of money? In this day we must be very careful about the expense we add by keeping a patient in the hospital for extra examinations The worry about expense and the ill effects on the bowel caused by worry will offset the information obtained from the 24 hour colon examination

Dr Wilbur Perhaps I might also add—a little extra radiation I would like to ask Dr Albronda if he would discuss the psychodynamics of constipation as he feels they apply to this case

Dr Albronda You might remember that in my previous presentation I mentioned points in the history which should alert to the possibility that psychological factors are of prime importance in the genesis of the patient s symptoms These points are Shifting complaints a family history of emotional instability evidence of nervous tension in childhood poor school and vocational record long medical history which includes often numerous operations many contacts with physicians disturbances in sexual relationships and current signs of nervous tension with or without the presence of significant organic disease

It seems to me that the case report we have heard contains data in at least seven of the eight categories just mentioned

1 *Shifting Complaints* In addition to constipation—headaches dryness of the mouth pains in the shoulders and back of the legs severe nausea retching dizziness and faint feelings were mentioned

2 In her *family history* we find evidence *of emotional instability* Father has asthma and peptic ulcer mother had constipation until age 40 Aunt had constipation One brother had peptic ulcer One sister had asthma, another constipation

3 *Signs of Nervous Tension in Childhood* The case report mentions that in childhood the patient had been taken to several doctors for the treatment of constipation without any lasting relief

4 *A Long Medical History and Often Numerous Operations* She fills at least half of this category How she missed being operated upon is a mystery to me! Most of the patients I have seen in consultation for this complaint have had operations They describe exploratory operations uterine suspensions appendectomies caesarean sections and cholecystectomy

5 *Many Contacts with Physicians* This is self evident from the record as is her disturbance in *sexual relationships* and *signs* of nervous tension

I suspect that if she were questioned carefully about her *school and vocational history* we would also get data suggestive of psychological factors being important such as absence from school because of illness over or under participation in the school social activities considerable uneasiness perhaps with diarrhea or constipation around examination time

Other points in the case report which to me are suggestive of psychological difficulties are (1) convulsions and frequent fainting spells in 1948 (2) her almost addiction to laxatives (3) chronicity of her complaints

I would have no hesitation in recommending a psychiatric consultation for this woman There is not enough data in the case report to formulate the psychodynamics but I suspect data could be obtained by skillful interviewing that would enable us

to do so It only points out again at least to me that this patient s psyche has been s idly neglected over a period of at least 21 years Please understand that I am not blaming the physicians! How can they be blamed when they were not taught to consider the importance of the psyche in the total examination of the patient?

Dr Wilbur Dr Simpson will give us some information about the central nervous system

Dr Simpson To refresh our minds on the relation of the central nervous system to bowel function I would like to show a diagram The motor innervation of the intestinal tract goes through the vagus The vagus originates in the medulla and travels a long distance As you know it branches to the stomach small intestine and the other gastro-intestinal organs—the liver the pancreas and to the right part of the colon Most of our evidence is that the right colon motor and secretory innervation comes through the vagus and extends as far in the right colon as is supplied by the superior mesenteric artery In some people it extends to about the mid transverse colon In most people it extends as far as the splenic flexure The other part of the colon and the rectum is innervated through the 2nd 3rd and 4th sacral parasympathetic following along the supply of the inferior mesenteric artery At the lower part of the colon the sacral parasympathetic has to do with the motor activity of the rectum and the complicated function of relaxing the internal anal sphincter Now the other part of the nerve supply to the intestinal tract especially the colon the sympathetic is derived from the T 11 T 12 L 1 L 2 and sometimes L 3 These fibers supply the colon from the ileocecal junction to the anus and have to do with increase in sphincter tone All through the G I tract the sympathetic increases tone and relaxes muscular activity just the opposite of the parasympathetic system In all cases of functional disturbance it isn t simple disturbance of one or the other innervation These are always mixed We cannot purely and organically separate out which function is at fault Generally there is an inhibition of motor activity so nothing passes along

Now what carries on peristalsis in the colon? It is the myenteric or Auerbach s plexus which usually keeps up peristaltic move

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fact that the colonic wall contains the myenteric plexus to which Dr Simpson just referred It is believed that the myenteric plexus conducts the stimulation and coordinates the movements of the intestinal wall Absence of these plexuses might lead to decreased contractions of the muscles as for instance in Hirschprung s disease which seems to be due to absence of the myenteric plexus It seems possible that many substances which incite intestinal movement do so by stimulating the cells of Auerbach s plexus These substances might be chemicals liberated from the food or by bacterial action or they may be chemicals used in therapy The colon is liberally supplied by these plexuses which may also serve for transmitting the vagal impulses to the bowel Propulsion of the feces involves increased motor activity over most of the large bowel It is believed that activity gives rise to the call of nature rather than the presence of feces in the rectum Contraction of the colon may be brought on by ice application to the abdomen and by a number of drugs like physostigmine neostigmine posterior pituitary extract Pitressin® amyl nitrite nicotinic acid and also by emotional factors Emotions like fear dejection defeat, dissatisfaction boredom tension and a sense of futility may be associated with a hypodynamic situation characterized by a relaxation of the longitudinal muscles and lengthening of the colon and decreased motor activity However emotions like anger resentment guilt feeling anxiety and strong conflicts are usually associated with a hyperdynamic motility state of the colon in which there is usually contraction of the longitudinal muscles and shortening of the colon and increased rhythmic contraction of the circular muscle This autonomy of the colon is being exploited therapeutically and substances are being introduced which stimulate the colon either directly through Auerbach s plexus or directly through the mucosa without interfering with the activity of the small bowel

Dr Wilbur Well I think we have a little information about certain basic mechanisms It would be appropriate to ask Dr Alvarez if he would tell us using the information we have available how he interprets the psychological disturbances in their relation to this young woman s disturbed colon function

ment One of the main functions of the whole G-I tract is trans portation and motility In the colon after water is absorbed the left colon is primarily concerned with transportation and motility If we could just apply a drug to stimulate Auerbach s plexus through the vagus nerve it would be wonderful but things don t work out that way clinically Increased parasympathetic stimula tion above a certain point doesn t produce increased peristaltic movement but spasm so that forward motion disappears alto gether and constipation is the end result

Then there is a factor of relaxation of the anal sphincter the internal sphincter has something to do with it The ileocecal sphincter may have possibly a very little effect

The hypothalamus should be mentioned This area receives from the cortex and from the outer environment all those stimuli that Dr Albronda made so clear to us this morning I think that covers the general anatomic structure and function of the bowel from the viewpoint of the present discussion

Dr Wilbur We have now a little information about the psyche and about the means by which it may influence the function of the colon Dr Steigmann is going to give us a little information about how the function of the colon may be altered and about the mechanisms of intrinsical neuromuscular activity which cause the colon to move

Dr Steigmann I do think it is somewhat presumptuous for me to discuss the functions of the colon when we have here Dr Alvarez the man who did most of the work on that

The colon is a sluggish organ with few movements and slow movements A few times a day there are mass movements that carry the fecal material from the transverse colon into the sigmoid region These mass movements may give the so-called call to defecation The mass peristalsis often takes place during or im mediately after a meal the so called gastrocolic reflex Usually in the morning after breakfast the colon starts the mass peristalsis movement

Mass peristalsis may also be introduced by purely psychological influences The colon can perform its function to a great extent independent of the central nervous system This is due to the

of family I was dealing with Naturally I didn t cure the woman at all I would have to start with a different set of ancestors

Now what I am very much interested in in this woman is what these falling spells are like You notice I asked her if she hurt herself If they hurt themselves it is generally epilepsy If they never hurt themselves it is generally just fainting An epileptic injures himself or nearly always hurts himself Now the thing that impresses me is that we never bothered to get an electroencephalogram on a woman like this The last eight to ten years I have been getting electroencephalograms and I am finding that about 60% of these people are epileptics who never had a very typical fit and perhaps hardly ever had fits at all Now does that have any relation to her constipation? Yes I m absolutely sure because I find some of the most remarkable abdominal complications in people who are epileptics without a fit Hughlings Jackson described any number of epileptics without fits It was well known 75 years ago and today it is hardly known at all Epilepsy is one of the things we should study about this woman I think

Dr Wilbur Well that is very interesting However I would like to come down to this very practical point and that is why is this woman constipated? I would like to ask members of the panel why her colon doesn t work satisfactorily Is this some disturbance intrinsic in the colon itself or is it something that comes from outside the colon in the way of the influences of the psyche that Dr Albrondi talked about, or through these nerve pathways or is it all three? How do these psychic disturbances produce constipation? If we don t know why she s constipated how can we treat her?

I thought someone would tell me that she had a disorder of her type 2 waves or that she never had a type 4 wave and therefore never had a mass movement in her colon I think the time will come when someone who is interested in the physiology of the gastrointestinal tract will make studies on a patient of this sort and have information available as to just what causes the disturbances in the colon that makes her constipation as long as 30 days without a bowel movement

Dr Alvarez Usually when I see a woman like this my first question of course is has the patient mild megacolon? Obviously this woman hasn t Most of them haven t The next question is is it hereditary?

The fact that she has had it for over 20 years immediately tells me that she hasn t carcinoma or anything blocking the way Where is the lesion? Is it in Auerbach s plexus or is it in the extrinsic nerves? In megacolon as you know it is in the intrinsic nerves In megacolon there is a section of the sigmoid or rectum which contains no Auerbach plexus or practically none which is why waves can t go over it and that s why the Swenson operation is a good operation in that the involved section is removed

Now there is a point that impresses me about these women All of them that I have gotten to know well and could get the family history in all of them I have found psychosis or epilepsy or alcoholism running through the family—a defective family In this family we know that there is a good deal of nervousness It has come out in the form of asthma I think if we question her very carefully we might learn of more serious illness What does that mean? All I can tell you is that from hundreds of cases I have learned that insanity in grandfather may show up as a defect in sympathetic behavior in the grandson I have seen it and I have just written a book on about 1000 such families showing the remarkable ways in which defects in the nervous system are inherited For instance a girl may complain of cyanotic legs and a lot of other symptoms You find her father is a schizophrenic and is in the state hospital There is some relation between these two facts and I see it commonly I have seen it so many hundreds of times that I can t question it at all

A very important thing in these women is that they say they can t take an enema—it burns me all the way up or else they can t get it in The reason they can t get it in is because they can t stand a little distress The last one of these women I had spent between two to four hours a day trying to get a bowel movement Well what is her family? Her mother was a devil Her grandfather was crazy her father was crazy her husband had deserted her and I think she had two psychotic sons That was the sort

of family I was dealing with Naturally I didn t cure the woman at all I would have to start with a different set of ancestors

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Dr Alvarez Years ago Ivy and one of his students introduced a balloon up through a sigmoidoscope and found different types of records in this type of patient

Dr Wilbur I believe that some of the newer methods of recording motor activity in the gastrointestinal tract without a balloon will be more helpful Perhaps 10–20 years from now when such a panel as this is held very definite information will be available as to exact motor disturbances of the bowel in constipation

Dr Farrar We have studied now three people with constipation and two of them had what seemed to be records not significantly different from some of our normals One had rather abnormal looking waves We're not in a position to tell yet but certainly it is relatively easy with this capsule to get a tracing throughout the entire colon and we hope to have some data within a year

Dr Hightower We have also studied some of these patients but we were not able to detect what we think are significant changes from normals I think these newer techniques do have possibilities in elucidating some of these factors in constipation

Dr Wilbur Dr Templeton how much can the radiologist help the clinician in determining function of the colon particularly in a situation of this sort?

Dr Templeton We are limited We do have the occasional patient who cannot be cleaned out We give cathartics and enemas and after three or four days the patient still has material in his colon The reason we cannot clean him out is that we cannot stimulate a mass peristaltic wave We produce some tonic contractions but these are not enough to force the material along As to the reproduction of the pain sometimes we can help out a little bit on that We haven't been able to do it too often but occasionally we can That's about our limit

Dr Alvarez This problem fascinated me Many years ago the thing that gave me ideas was a picture by a man named Bederman back in the 60's who cut the nerve from the central nerve cord of a snail where the smooth muscle comes off to the side Immediately those muscles contracted into a knot and

stayed that way and I thought that would be the simplest explanation for the troubles in the bowel I hunted through the literature particularly of pathology to see if I could find a record of a segment of a bowel which contained no Auerbach s plexus and to my great joy I found an article in an Italian journal on pediatrics describing two boys and if I remember correctly they were twins both of whom had megacolon and in whom this piece of apparently obstructing bowel was resected It wasn t contracted and there was found absolutely no Auerbach s plexus and so my hunch was proven correct and since then has been proven many times by Swenson I just noted a report of 158 cases from England and the results in removing the paralyzed segment had been pretty good

Dr Wilbur I want to point out that in this patient however there is no sign of any nerve cutting no sign of any disease of nerves or of the colon but only the colon doesn t work as a normal colon should function

In the remaining minutes I think it would be well to discuss the treatment of this condition the cause of which we haven t been able to define I am going to ask Dr Albronda what he thinks a psychiatrist could do in approaching this patient diagnostically and whether he thinks that psychiatric treatment would be helpful for this young constipated woman

Dr Albronda Before we can figure out what to treat psychiatrically we have to study the patient very very carefully and from a practical point of view With this lady I would strongly advise the internist to refer the patient for a psychiatric consultation Now very often the internist needs help in referring such a patient for psychiatric consultation because most patients will say "There isn t a thing the matter with me I am not crazy Why should I see a psychiatrist for my constipation? Sometimes some explanation about how feelings play a part in a patient s difficulty will reassure them enough so they will consent to such consultation Then the psychiatrist will try to figure out whether or not psychological factors are playing a part in the difficulties Sometimes such a person is reluctant to give this kind of information as Dr Alvarez so well pointed out and Dr Steigmann men

tioned We often use the clinical psychologist for psychological testing of the patient who may help us come to some conclusion If the person is found to have some psychiatric difficulties that are playing a part in the complaints then the next step is to find out whether the patient is willing and desirous of having psychiatric treatment This is often a big hurdle to get over but often it can be done If it is clear that psychological difficulties do play a part in the persons difficulties and if he is willing to have this particular kind of treatment I think the appropriate treatment is psychological and often preferably in collaboration with the internist

Dr Halpern From a pharmacologists viewpoint my interest was directed to the problems of drug therapy When a drug is administered it is important that it is used early enough long enough often enough and just enough It is necessary to treat the patient and not the disease You cannot take a drug and administer it by rote or by labeled directions The use of a drug should be adapted to the patients requirements It is important to remember that the medication does not want to superimpose another set of physiologic negative conditions For example if you are treating constipation it is not correct to superimpose diarrhea The appropriate considerations of the properties and dosage of a drug will result very often in a satisfactory approach to both the patient and the disease problem

Another factor is to consider the over all aspect of drug therapy and constipation For example ganglionic blocking agents are constipating antacids are constipating sedatives tranquilizers except reserpine are constipating Reserpine causes a diarrheal state in some Barbiturates hypnotics morphine and opiates all have constipating properties Now if you are going to treat constipation as an isolated phenomenon you are going to get just the type of result that you deserve If you are going to treat constipation as a part of the complete picture of the patient you will probably get the result which is hoped for

There is still another point to be considered and that is the reliability of the drug you are going to use You have to know certain things about it You have to know of its reproducibility

Will the drug that you are administering be the same drug that you hope is described in the literature? By that I mean is it stable? Has it been standardized? Is the variation from dose to dose such that it will give bizarre results? It is obvious that the clinician cannot turn his office and his pharmacy into a testing laboratory That means you have to have some understanding of the companies who make the drugs and some understanding of their testing procedure because this is really a partnership operation The practice of medicine is no longer confined to the clinician It becomes a hand in hand partnership with everyone involved in community health

Dr Wilbur I am sure all of you would like to hear how Dr Alvarez would treat this patient

Dr Alvarez I have already confessed that I am not very successful in handling these people usually

Dr Wilbur Is there any point in treating her at all?

Dr Alvarez I think it is necessary to try to treat her constipation because when she goes too long she gets marked reverse peristalsis even to the point where she gets vomiting and dehydration so something must be done Sometimes in these people I help them most by getting them to be fairly satisfied with a bowel movement once in every ten days if they are not too uncomfortable In other cases one can find psychological reasons for her constipation Maybe she doesn t go when she should or maybe she doesn t eat properly or all sorts of things that you can alter to try to help her along In most of these cases the people are so basically unstable that it is very hard to do anything with them

I would use laxatives such as the one that she found magnesium carbonate Many of my patients of this type tell me that is the one that they wind up with as being the least offensive and least trouble

Dr Simpson I think that this patient must be treated as a whole So far we have covered many little segments of her problem and now we are closing in on what ought to be done for this lady before she leaves your office and goes on to another doctor I think the first thing to do is to go through the history and that

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DISTURBANCES OF GASTROINTESTINAL MOTILITY ASSOCIATED WITH SYSTEMIC DISEASE

J ARNOLD BARGEN MD

IT has frequently been observed that motility disturbances of the digestive tract mirror disturbances of the body generally Everyone is familiar with the severe vomiting attack that is initiated by some emotional disturbance and the vomiting associated with serious systemic disease It is as if there is an attempt to release abnormal bodily accumulations by reverse peristalsis thus freeing the body of its poisonous substances A vomiting center seems to have been designed for this purpose

Just as certain systemic illnesses are associated with vomiting so also are many others associated with hypermotility of the intestinal tract and with diarrhea Nearly everyone is familiar with the hypermotility of the digestive tract that frequently is associated with emotional strains and tensions Thus the religious leader often is afflicted with diarrhea every Saturday and Sunday the motility of his bowel is quite normal the rest of the week This has frequently led to the fallacious diagnosis of colitis when diarrhea is meant Emotional reactions resulting in disturbed intestinal motility may be confused with real inflammatory conditions Thus patients with the so called irritable bowel syn

Professor of Medicine Mayo Clinic and Mayo Foundation Rochester Minnesota (The Mayo Foundation Rochester Minnesota is a part of the Graduate School of the University of Minnesota)

is part of her psychological treatment We wondered where the lesion was and we haven t found it To me it appears to be some where in the complex reflex mechanism of the motor activity of this gut—both psychic and physiologic Most of our work as clinicians will be sitting down with her and trying to untangle all that has gone on in the past—both psychiatric and organic from enema laxative and other bad habits

Dr Wilbur Here then is a problem of a patient who has con stipation who actually has only one manifestation of a disturb ance and that is of her psyche as Dr Albronda has pointed out We don t know why her colon is disturbed or how its function is disturbed but we are all convinced that the treatment of the constipation alone is not going to be successful that the patient as a whole must be treated In this respect a sympathetic phy sician is probably more useful than anything else Every once in a while one does see a patient of this sort who is suddenly cured Dr Bargen tells of a patient who had constipation of this sort for many years and who during an earthquake saw the earth open up in front of him He hasn t had constipation since that time If one could work out some sort of mild shock therapy for this patient perhaps her constipation would be cured

In conclusion I recall a statement of Josh Billings which I think is appropriate here and that is A good reliable set of bowels is worth more to a man than any quantity of brains

descending colon in a manner that is more or less startling to the unaccustomed observer

The extent and manner of nervous control and innervation of the digestive tract are not always the same from person to person Generally speaking autonomic effects are inhibitory in character and diffuse in distribution The results of surgical operations to remove inhibitory control have been disappointing That these procedures have not been as effective as it was hoped they would be has been especially clearly demonstrated after surgical operations *however well performed on the lumbar sympathetic* nerves in cases of advanced megacolon It may be that the autonomic nerves are called into action only in an emergency, for instance in such states as fear pain dehydration and shock of one kind or another Stimulation of the sacral division of the parasympathetic system results in contraction of the bowel with relaxation of the anal sphincters Any emotion that is accompanied by nervous discharge through the autonomic system may also be accompanied by effects mediated through the sacral division of the parasympathetic nerves The distribution of vagus nerves of the lower intestine is not certain The profound effect of psychic stimuli in the field of vagus control can hardly be disputed In the presence of megacolon atrophy and dissolution of the plexuses of Meissner and Auerbach have been observed and in the presence of advanced ulcerative colitis there is a suggestion that great hypertrophy of the ganglion of these plexuses has occurred

It has long been recognized that the secretory activity in the intestine has considerable bearing on the abdominal discomforts of human beings The importance of this function is well attested to by the many designations applied to disturbances of it such as "mucous colitis and the many synonyms used to describe this or similar phenomena

EMOTIONAL FACTORS IN COLONIC MOTILITY AND SECRETION

The anxiety present in everyone most of the time may profoundly affect motility and secretion in the digestive tract Tense emotions involving marked anxiety are often accompanied by

drome labor under the mistaken belief that they have colitis Patients with both of these conditions may have diarrhea Unless the intestinal tract of everyone with diarrhea is examined carefully and objectively many unfortunate errors of diagnosis and therapy will result

I shall evaluate some of the studies of motility patterns of the digestive tract in the light of its structure and function and shall show how knowledge of these patterns may lead to better management of disorders of the digestive tract in its various disease states or in conditions due to disturbed function

FUNDAMENTAL OBSERVATIONS

Man s digestive tract has features that correspond to those of Carnivora and to some of those of Herbivora It is large and distensible and retains its contents for a relatively long time It consists essentially of floating organs Its position in the abdomen varies with posture respiration and degree of distension Its kinks redundancies and fixations are only variations of the normal but compatible with healthy living.

Knowledge of the alimentary tract has been greatly enhanced by the development of applicable roentgenologic technics Observations of roentgenologists on its physiology and pathology have laid the foundation of present day knowledge The time of passage and the size of the column of barium as it proceeds along the intestinal tract vary greatly among persons who to all intents and purposes have normal intestines More than likely then the same thing can be said about the passage of food residue down the same tract The process of colonic filling for instance seems haphazard There are almost as many variations as there are persons Food residue follows a pattern similar to that of a suspension of barium It is easy to understand why the former may reach the left portion of the colon in one person in 30 minutes and that of another in 5 hours without it being necessary to assume that abnormal conditions afflict either person In the large intestine in addition to the mixing and kneading that go on continuously there is another type of movement known as mass movement of the contents wherein by a single large contraction the entire colonic content is caused to pass into the

inflammatory disease Furthermore there is no evidence either clinical or experimental to suggest that these disturbed emotional states ever produce an actual organic change in the intestine In some patients during unusual psychiatric stimulation hyperemia or even edema, and evidence of congestion have been produced in the intestine These promptly subside when the existing stimulus is removed Thus it is apparent that all portions of the digestive tract may participate in the reaction pattern that results from unfavorable or unpleasant situations

It has been possible to establish this situation experimentally in regard to the secretion of mucus The colon of an anesthetized dog was isolated by sectioning the distal part of the ileum and sectioning the colon as near the anus as possible End to-end anastomosis was made between the proximal part of the ileum and the distal part of the colon The distal end of the ileum was then brought outside the abdominal wall on the right side and the proximal end of the colon was brought outside on the left leaving the isolated portion which was nearly all colon, in the abdominal cavity with its nerve and blood supply intact The volume of mucus secreted from such an isolated colon when the dog was lying quietly for several hours at a time was fairly constant and tended to be less the quieter the animal remained During sleep secretion was at its lowest level although at no time did the stoma become dry Ten to 15 minutes after a spontaneous bowel movement without a purgative having been administered or stimulation of any kind having been given an increased amount of secretion appeared at the opening on the left side and exudation continued for about an hour although the largest globules of mucus appeared at first

Cathartics such as senna rhubarb phenolsulfonphthalein mild mercurous chloride sodium sulfate colocynth and castor oil were administered by mouth to dogs with the colon prepared as described The amount of secretion obtained from the isolated segment was much greater after the administration of these cathartics than it had been when defecation occurred without such stimulation Saline cathartics produced amounts of mucus most closely resembling those of control animals Of all these

physiologic changes After a state of anxiety is repeated often enough it subconsciously may be manifested by unusual functional bodily states resulting in many vague unrelated complaints associated with physiologic disturbances of organs and organ systems Thus profound effects of emotional states are registered in the gastrointestinal tract At times even a single severe emotional impulse causes striking change in functions of an organ A person who has always been constipated may have a disturbed intestinal function with frequent passage of loose stools as a result of a severe accident, a state of fear or some other emotional upset In this way an episode of fear sudden and unwanted as it is can be an effective drugless remedy for constipation

The effect of excitement and tension on the gastrointestinal tract is common knowledge The emotional effect of excitement and tension may be transient but if these distresses are frequently repeated a tension state may develop and result in a marked change in intestinal function The culminative effect on the secretion of acid and pepsin in the stomach is well recognized But this secretion may be greatly increased or reduced by nervous and emotional disturbances Increased motility and decreased absorption in the small intestine during an emotional state are also well recognized phenomena

The terms irritable colon and unstable colon are only names expressing the effects of emotional disturbances excesses acts of abuse or traumatic experiences on the intestine The syndrome described as the irritable colon or unstable colon does not actually refer to changes in the colon itself but its symptoms are manifestations of overactivity or reduced activity of the entire digestive tract The so called irritable colon may also be a result of dietary indiscretion There is no evidence that it is ever followed by or related to actual intestinal disease As indicated previously many gastroenterologists have seen the church leader the priest or minister the lawyer or the public speaker who prior to or during an important address is afflicted with intense diarrhea This state promptly subsides after the emotional strain has been relieved In none of these individuals is there any evidence of

to the transducer situated just outside the mouth The pressures detected by these devices are those occurring within the lumen of the esophagus and in the immediate vicinity of the unit When the esophagus is relaxed and patent the changes in pressure may be those common to the entire length of that organ When the walls of the esophagus or its sphincters are in direct contact with the pick up unit changes in pressure that it detects are localized to the segment that is in proximity of the unit The wall of the esophagus is regarded as a muscular tube that is closed at both ends by sphincters this tube and its sphincters operate as a functional unit that responds in a coordinated manner to deglutition or esophageal distension

In the resting phase the pharyngo-esophageal sphincter is represented by a zone of increased pressure 2 to 3 cm in width lying between the upper part of the esophagus and the pharynx This zone can be clearly delineated by withdrawal of a pressure sensitive device from the upper part of the esophagus into the pharynx As withdrawal progresses the pressure increases until it is 20 to 30 cm of water greater in the upper portion of the zone than in the upper part of the esophagus As the device is withdrawn farther the pressure decreases abruptly as the unit enters the pharynx During the act of deglutition pressure in the gastroesophageal sphincter decreases indicating relaxation The relaxation occurs early in the sequence of deglutition It persists until the peristaltic wave reaches the sphincteric zone Then in sequence with the peristaltic contraction of the esophagus the pressure in the sphincter increases to a level greater than that encountered at rest A gradual decline to the resting value follows The sequence indicates that the peristaltic wave enters the sphincteric zone and closes the sphincter by a contraction that is more prolonged but of less magnitude than that in the esophagus proper

These methods have proved valuable for study of the mechanism of swallowing in patients with achalasia diffuse spasm of the esophagus scleroderma and other esophageal abnormalities Resting pressures above and below the hiatus have been measured in expiration and inspiration The important difference

cathartics castor oil produced the most sustained and most constant increase of secretion many hours elapsed before the activity of the isolated portion of the colon ceased When diarrhea developed a definite increase in the amount of mucus secreted from the isolated portion of the colon followed During pregnancy the amount of mucus secreted from the colonic stoma was consistently greater than it had been before When a dog was placed at rest for several weeks, the isolated portion of colon filled with a mucous cast When such a colon was exteriorized and opened longitudinally leaving the mucosa exposed the secretion of mucus was observed at all times Droplets of mucus were seen to appear on the mucous membrane giving the appearance of dew on grass

These experiments indicate that the secretion of mucus is a physiologic phenomenon It is the normal response of the colon to activity of one kind or another when this activity is excessive it results in exaggeration of the protective response of the mucous membrane to an abnormal stimulus either acting locally in the bowel or reflexly from other organs through the channels of emotion or through any form of irritation This it seems to me *stresses the fact that application of the term colitis to such a* condition is unwarranted These observations should constitute the final chapter in elimination of the popular term mucous colitis

MOTILITY STUDIES IN SEGMENTS OF THE DIGESTIVE TRACT

Observations of the motility waves in various segments of the digestive tract could throw considerable light on functions of segments of this long floating tube in states of health and disease and thus point the direction of therapeutic endeavors

Motility Studies of the Esophagus Motor activity in the esophagus and its sphincters has been determined by measurement of intraluminal pressures This has been accomplished by the use of tiny electromagnetic pressure transducers The unit is swallowed by the subject and localized in the esophagus or the subject may swallow water filled tubes that are connected

The results of the studies were analyzed on the basis of numbers of types I II and III waves produced Each of these waves has been well described by Code Hightower Templeton Ivy and others Type I waves are those of low amplitude varying in duration from 18 to 22 seconds Type II waves are of greater amplitude than type I Type III waves are more complex They consist of two components a series of rhythmic type II waves superimposed on an increase of basal pressure

Motility waves were present only 38 per cent of the time this was divided between type I and II waves type I 23 per cent type II 15 per cent Type I waves were in rhythmic pattern about half of the time Type II waves were in rhythmic pattern about one third of the time Type III waves were rarely recorded being present during only 1 per cent of the period of observation Neostigmine given intramuscularly to some of the subjects produced only a slight increase in the duration and height of the nonrhythmic type II waves

In the same way studies of the effects of bethanechol chloride (urecholine) on antral gastric motility in individuals who had vagotomy or peptic ulcer were made The effect of the drug was evident on the record of gastric motility This drug increased total activity by increasing the number of type II waves in every instance The amplitude of these waves was also significantly increased Decrease or absence of gastric motility in patients after vagotomy has been amply demonstrated clinically The apathy and hypomotility that occur after this procedure at times produce troublesome gastric retention This study indicates in an objective manner that urecholine stimulates gastric motor activity in human beings after vagotomy and promotes emptying of the stomach

Motility Patterns of the Duodenum and Jejunum Studies of the motility of the duodenum and upper part of the jejunum made on normal persons by Foulk and his associates showed periods of activity alternating with periods of quiescence In the beginning of an active phase single type I waves appeared with progressively diminishing periods of quiescence between them until groups of these small waves were present in sequence Relatively small and brief type III waves then often appeared

between healthy volunteers and patients with achalasia is that resting pressures in the esophagus in achalasia are frequently abnormally high The high esophageal pressures are associated with dilatation of the esophagus and retention of food and secretions

Diffuse spasm on the other hand is characterized by incoordination of the responses of the lower part of the esophagus to deglutition and esophageal distension Simultaneous and prolonged contraction of the lower part of the esophagus with swallowing is a salient physiologic finding The physiologic appearance of curling of the esophagus is the result of the forcing of barium into the zones of lesser resistance or strength by the vigorous contraction of the whole affected zone There is no physiologic evidence of alternating rings or segments of contraction and relaxation Extreme pressures developed in diffuse spasm are likely the consequence of the muscular hypertrophy that has been demonstrated in this condition

Two abnormal features of esophageal motility in the presence of scleroderma that predispose to the development of symptoms and clinical findings are the loss of tone of the gastroesophageal sphincter and the loss of contractile power in the lower three quarters of the esophagus the loss of tone allows regurgitation of gastric content and the loss of contractile power renders that portion of the esophagus powerless to react and thereby to expel the foreign material Studies of esophageal motility have taught us much about the esophagus in health and disease

Antral Gastric Motility With a water filled but undistended balloon placed in the antrum of the stomach and connected to a glass spoon manometer that records the pressure in the balloon on moving photostatic paper gastric motility was studied in 25 normal subjects The subjects fasted from 15 to 18 hours before observations were made After intubation the balloon was localized in the antrum of the stomach by roentgenoscopic observation and the tube was anchored to the face Subjects were then placed in a supine position on a comfortable cot in a quiet room Observations of motility were made in 1 to 2 hours The records so made were studied from the standpoint of the type of waves produced

stomas Indeed the passage of material through the stomas was used as a measure of occurrence of propulsive motility Two balloons were inserted into the distal part of the ileum for a distance of about 30 to 35 cm from the stoma. The studies were carried out after an overnight fast The patients lay quietly on a couch during the period of recording which usually lasted 2 hours or longer Many periods of study were devoted entirely to observation of the motility pattern after an overnight fast, which ranged between 10 and 16 hours Meals drugs and placebos were given after a 1 hour control period Observations of motility were made continuously while the meal was being eaten and then for an hour or more thereafter

Drugs broadly classified as cholinergic anticholinergic and narcotic were administered When drugs were administered *hypodermatically* control injections consisting of saline solution were also given so that when the subjects came for observation they did not know the nature of the test or the substances administered

Activity was present about 90 per cent of the time in both balloons throughout the first and second hours of the fasting observations and during the control hour preceding administration of the drug meal or placebo The percentage of time during which activity was present in the first hour of the fasting studies was not significantly different from the percentage during the control or first hour of the other studies There was however a tendency for the amount of activity to be reduced in both balloons during the second hour of the observations made after fasting

The rate of occurrence of type I waves in rhythmic sequence in the small bowel has been referred to as the basic rhythm of this portion of the gastrointestinal tract Type I waves were present almost continuously throughout the records of both subjects Type III waves were present about half of the time in one of the subjects and about one third of the time in the other There were also waves of the type seen in the colon namely type IV which occurred as a smooth rise and fall in pressure These usually were present in both balloons the waves occurring simultaneously only slightly out of step one with the other Type IV

If activity continued, they usually became more frequent and prolonged Activity might reach a crescendo with a type III wave of several minutes duration terminating the active phase In normal persons who had fasted overnight motility was present from 60 to 70 per cent of the time Long periods of quiescence were unusual If a normal person fasted from 24 to 36 hours a marked decrease in activity of the upper part of the small intestine occurred The mean percentage of time during which activity was present was only 30 instead of 60 per cent or more In patients with duodenal ulcer there was an increase in the percentage of time during which this basic rhythm was present In patients with ulcerative colitis the amount of the basic rhythm was decisively increased Bursts of basic rhythm occurred consistently in the records of patients with ulcerative colitis and they were present for longer periods than those obtained from normal persons Basic rhythm constituted three times as much of the period of observation in patients with ulcerative colitis as in a normal subject

Such studies give fundamental knowledge of changes in the motility pattern of the upper part of the digestive tract in normal persons and in those with disease of this tract Only preliminary studies have been made It is reasonable to hope that they have opened a vast field of interest

Motility Patterns of the Ileum Detailed observations of ileac motility have been made in patients with ileac stomas created because of ulcerative colitis Two patients volunteered to be studied for an entire year Both were men 27 and 38 years of age respectively Their ileac stomas had been constructed within 30 cm of the ileocecal valve One patient had undergone complete colectomy but the other still had his colon intact The time available allowed for numerous observations under fasting and postprandial conditions and afforded an opportunity to test the effects of a variety of drugs A tandem balloon photokymographic method of recording motility was used throughout the investigation Balloons employed in this technic are of very small capacity They did not offer an obstruction to the content of the bowel since material flowed freely around them and appeared at the

IV waves Other factors besides obstruction stimulate the development of such waves In our study they occurred after the ingestion of a meal or after the administration of drugs with a cholinergic action. The ileum of each patient was regarded as normal at the time of creation of the stoma In neither case had colitis extended into the small bowel

It is reasonable to assume then that type IV waves in the terminal part of the ileum represent a form of normal physiologic motor activity and have a propulsive function They are closely related in form sequence and function to type IV waves of the colon The tremendous propulsive or expulsive force of the waves suggests that a contraction passes distally over the terminal part of the ileum but our records do not support such an interpretation. It seems rather that contractions are present in rhythmic sequence just after the ingestion of a meal transforming the ileum into a pump and forcing whatever it contains into the colon The development of type IV waves in the terminal part of the ileum following a meal is apparently part of the gastroileal reflex

It would seem then that morphine slows the passage of material through the small bowel. This is apparently due to reduced coordination between the motor action of adjacent segments or to diminished propulsive contractions In this study it was clearly due to fewer type IV contractions or to complete disappearance of them *The cholinergic blocking agents on the other hand* eliminated these contractions These drugs also reduced or eliminated all other types of activity Morphine reduced the specifically propulsive type IV waves while it stimulated other forms of motor activity The total amount of activity was not reduced The duration of type III waves may have been increased and the amount of rhythmic type of activity was greatly increased Type I and type III waves are apparently predominantly mixing and absorption aiding forms of motor activity of the small bowel Thus in general terms morphine stirs up the contents without taking them far while neostigmine not only mixes the contents but moves them distally

Motility Patterns of the Pelvic Colon and Rectum Quantitative estimations of motility in the pelvic colon and rectum of

waves occurred rather rarely in the records of these patients after fasting and relatively infrequently in the control periods They were usually seen in groups approximately four such waves occurred in one of the subjects and seven in the other in each hour Type IV waves developed considerable pressure in the balloon recording system A relationship existed between the occurrence of type IV waves in the records and increased passage of material from the ileac stomas Every time type IV waves were present some of the ileal contents were forced through the stoma Whenever the material came forth in gushes type IV activity was present

Ingestion of a hearty breakfast decisively altered the motility pattern of the terminal part of the ileum Type I activity was reduced and type IV increased A dose of 0 5 mg of neostigmine given intramuscularly produced striking effects very similar to those produced by a meal Injections of placebos did not have such an effect The patterns of response to cholinergic blocking agents atropine methantheline and diphemanil were identical In general the cholinergic blocking agents reduced the percentage of time during which activity was present

The effects of morphine were in marked contrast Total activity was not reduced The total amount of type I activity was unchanged but its distribution between nonrhythmic and rhythmic patterns was drastically altered There was a decisive increase in the amount of rhythmic type I activity The incidence of type III waves was not changed but the individual waves were somewhat longer in duration Type IV waves were reduced or eliminated The cholinergic blocking agents reduced all forms of motility morphine did not Morphine increased rhythmic type I activity maintained or increased type III and eliminated type IV

A striking difference between records of motility made in the upper part of the small bowel and those from the terminal part of the ileum is the occurrence of type IV waves Type IV waves correspond to the so-called large L waves described by Ingelfinger and Abbott These waves were not present in recordings of motility from the duodenum and upper part of the small bowel Obstruction does not seem to be the factor that produces type

ologic blocking mechanism that prevents too rapid aboral transport of intestinal contents it connotes a functional motor independence between two adjacent segments Intersegmental coordination is the phenomenon whereby the motilities of two adjacent functional segments become so integrated that the two segments act as a single motor unit

Our studies suggest that many of the so called antispasmodics given by mouth under prescribed dosage do not depress the tone and motility of the intestinal segments simultaneously except when atropine and ephedrine are administered together Atropine has been found consistently effective in either depressing or abolishing motility but it apparently has no demonstrable effect on tone Ephedrine in turn reduces tone without altering motility I could hardly advise that these two drugs be used together therapeutically however because of the side reactions inherent in each Many studies have been conducted to find a drug that would produce suitable sympathomimetic action such as that seen with ephedrine and a drug that would produce parasympathetic depression such as that seen with atropine without the production of unpleasant side effects Such drugs should be very helpful in the management of the host of individuals with a variety of irritable bowel syndromes

The effect of neostigmine on the motility of the bowel in persons with ileac and colonic stomas has been studied Motility has been recorded by means of tandem balloon systems connected with glass spoon manometers that record optically on a photographic camera The recording allows determination of the effect of neostigmine on the amount of activity present in the bowel types of contractions and their rate duration and amplitude and the coordination between contractions by adjacent segments of the bowel After intramuscular injection of 0 5 mg of neostigmine methyl sulfate an effect on the bowel was noted in 2 to 8 minutes This consisted of a definite change of character of the bowel activity The number of type I and type III contractions was decreased and the number of type II contractions was increased The average height of the type II contractions rose and the incidence of coordinated type II contractions increased The pro-

patients with ulcerative colitis have been made The predominant activity in the pelvic colon of the normal person is composed of type II waves sometimes scattered or occurring irregularly and sometimes almost rhythmic at the rate of 2 waves per minute Type I and III waves occur rarely and type IV waves are not seen From the records of patients with ulcerative colitis one gets the impression of a less active pelvic colon Type II waves are infrequent however type IV waves are common These are the type IV propulsive waves that are characteristic of the records of patients with ulcerative colitis but that are absent in normal persons The difference in motility between the normal person and the patient with ulcerative colitis can probably be explained by the loss of haustra in ulcerative colitis There appears to be general radiologic agreement about haustral movements of the large intestine The so called type II waves probably represent this type of activity In severe ulcerative colitis the haustra are lost hence there is a decisive reduction in type II waves Type IV waves are the propulsive type The high incidence of these waves in patients with ulcerative colitis no doubt has a causal association with their diarrhea There is no contradiction in the statement that there is less motility of the lower part of the colon in patients with ulcerative colitis than in the normal individual for this statement refers to the total number of waves of all types not to the occasional type IV propulsive waves

EFFECTS OF SOME DRUGS ON THE MOTOR FUNCTION OF THE HUMAN INTESTINE

The motor function of the human intestine has three basic components tone motility and the intersegmental relationships The resistance offered by the intestinal musculature to any distending force is commonly known as tone Those forms of rhythmic contractions and peristalsis that produce configurations of type I II and III waves on tracings obtained from the bowel are usually considered under motility The intersegmental relationships apply to the adjacent functional segments that comprise the intestinal tract and include both intersegmental coordination and incoordination Intersegmental incoordination is the physi

in chronic ulcerative colitis is increased approximately threefold over the number in normal persons Even when allowance is made for the pathologic contracture seen in ulcerative colitis the number of ganglion cells is increased twofold The number per square centimeter in the segmental type of ulcerative colitis is less than in the diffuse type and the number in uninvolved portions in the segmental type of chronic ulcerative colitis is usually slightly greater than in the adjacent involved segments

No obvious explanation exists for this increase of ganglion cells It may be that the stimulus of ulceration and increased function of the colon causes these so called small underdeveloped nerve cells to enlarge and to become adult in type and function On the other hand it is possible but improbable that certain persons are endowed with more than the average amount of myenteric plexus tissue and that chronic ulcerative colitis may develop in some of these persons It is an interesting study and may have a direct bearing on the observation of the great increase in the type IV contraction in the distal part of the colon in ulcerative colitis

PRACTICAL IMPLICATIONS

Studies of intestinal motility such as those cited in normal human beings and in patients with pathologic states should open up a large field of investigation Attempts are under way to learn how various drugs produce their effects and how they produce inhibition and change the motility patterns of the gastrointestinal tract Only a few drugs have been studied Many others may offer more fruitful experiences in control of the many types of abnormal intestinal motility

It can be safely said that at least half the patients who enter the office of the average gastroenterologist have complaints that are due at least in part to abnormal motility of the digestive tract In the analysis of the laboratory studies on human beings ways and means should be found to control the symptoms of many more of them It is a very large problem I believe experimental studies such as those discussed might open the way to its solution

portion of each hour that the bowel was active was no greater after the drug was administered than before Thus neostigmine shifted motility toward propulsion which was indicated not only in the recordings but also by the expulsion of feces and gas *Apparently this drug can produce rhythm in the bowel* When such a rhythm occurs the recorded contractions of the bowel are exclusively those of type II In these studies these contractions were coordinated and were repeated regularly every 2 to 4 minutes Thus neostigmine in suitable doses becomes a valuable drug to increase the propulsive activity of the bowel On the other hand it apparently reduces the mixing action It does not seem to initiate activity of the bowel rather it changes the activity

Drugs that quickly abolish intestinal motility have come into demand Tetraethyl ammonium chloride is such a drug It blocks effectively the transmission of impulses across the ganglia of the autonomic nervous system Holt and his co-workers employing a roentgenographic technic observed that the drug produced a prompt decrease in gastric tone dilatation of the stomach, and inhibition of gastric peristalsis after parenteral administration In our experience the activity of the small and large intestine may be satisfactorily suppressed by smaller doses of the drug than are required to suppress activity of the stomach There are however wide variations in individual responses to the drug But such a drug without unpleasant side effects would be valuable for control of hypermotility and diarrhea

THE MYENTERIC PLEXUS IN ULCERATIVE COLITIS AND ITS EFFECTS ON INTESTINAL MOTILITY

Twenty years ago Robertson and Kernohan noted the absence of ganglion cells in the myenteric plexus of the lower portion of the colon in cases of congenital megacolon Surgeons including Swenson have taken advantage of this finding in the surgical management of this condition Ulcerative colitis on the other hand is the very antithesis of congenital megacolon in that over activity of the large intestine seems to exist Careful study has shown that the number of ganglion cells in the myenteric plexus

in chronic ulcerative colitis is increased approximately threefold over the number in normal persons Even when allowance is made for the pathologic contracture seen in ulcerative colitis the number of ganglion cells is increased twofold The number per square centimeter in the segmental type of ulcerative colitis is less than in the diffuse type and the number in uninvolved portions in the segmental type of chronic ulcerative colitis is usually slightly greater than in the adjacent involved segments

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FUNCTIONAL INDIGESTION

WALTER C ALVAREZ MD

To show how important in the practice of gastroenterology is the recognition of digestive upsets and abdominal discomforts of nervous origin I think all I need say is that I who started out 48 years ago as a stomach specialist am now interested mainly in neuroses and what I call minor psychoses and fitless epilepsy" Why did I change in my interests? Because during my 25 years at the Mayo Clinic I found that perhaps 1 in 3 of the patients who came from long distances suffering from weird and puzzling syndromes of the types not described in books had "negative findings What was bothering many of them most was a poor nervous inheritance Others had broken nervously because of a life full of strain anxiety unhappiness or fear What they needed was the sort of help that a good psychiatrist gives but since until after World War II at the Clinic we had only one neurologist devoting part of his time to psychiatry all of us in the gastroenterologic division had perforce to become psychiatrists of sorts

Some of us physicians have experienced digestive upsets of emotional origin Fortunate is the physician who under the stress of strong emotion has experienced "functional indigestion or abdominal distress Why? Because he will then be more understanding and sympathetic with his nervous patients With the good rapport that he will then have with them he will be able to help many whom otherwise he could not help

Tension spreads into both ends of the digestive tube I have

long had the impression that the tension which often spreads out from an overactive brain into the nervous system of the body will sometimes spread a short distance into the two ends of the digestive tube—into the esophagus and cardia and into the rectum and sigmoid segment—causing esophagospasm and cardiospasm above, and mucous colics below

The great importance of the vagal branch that supplies the upper part of the jejunum Very important I believe is the fact that most of the right vagus nerve runs down past the stomach to supply the first part of the jejunum Strong influences running down from a disturbed brain greatly to increase the tonus of the first segment of the jejunum must often cause ripples or waves to run both orad and caudad from this part of the bowel As a result nervous persons, when suffering from a panic of fear or from an acute attack of migraine or motion sickness are likely to suffer from the effect of ripples of waves coming up their stomach and esophagus perhaps to produce burps regurgitation nausea and even vomiting plus the effect of ripples or waves running caudad to produce one or more large bowel movements The point for the clinician to remember is that stimulation of any one segment of a muscular tube is likely to send off ripples both orad and caudad

Esophageal Spasm All of us have seen women who under great emotional strain developed esophageal spasm that the roentgenologist could see Others were found to have cardiospasm and many complained of the sensation of globus which may possibly arise in the esophagus I think it is worth noting that when I studied the symptoms of 574 neurotic persons all of whom were descendants of psychotic or alcoholic persons I found 5 per cent suffering from nervous difficulties with swallowing

From now on I will be talking every so often about the frequency of the symptoms complained of by these 571 persons whom for convenience sake I will call relatives I have written up their troubles in my book *Practical Leads to Puzzling Diagnoses Neuroses that Run Through Families* (Lippincott 1958)

Air gulping and Repeated Belching Every physician should know that bouts of belching which lasts for a half hour or more represent a neurosis and not an indigestion Such belching is produced by air gulping and is often the result of a panic of fear or anxiety It is interesting to me that of the 574 "relatives" 17 per cent or 1 in 6 complained of distressing attacks of air gulping

One day I was asked to see a somewhat goofy" old farmer with a low I Q For weeks my assistant had been treating him unsuccessfully for "belching with diets belladonna soothing aluminum preparations and synthetic anti spasmodics When I asked him what brought on his spells of air swallowing he said Getting scared For instance when my brother and I are going slowly along the highway in our little old car and someone in a big car whizzes past us we get so startled and scared we have to draw over to the side of the road and stop There we belch and belch and belch Their mother was a very excitable woman with 2 insane brothers

In some of the cases of belching in which the patient is sane and intelligent the physician can work an immediate cure by first showing the person what he is doing second giving a sedative such as Bromural® or Butisol Sodium® and third insisting that he just stop the gulping much as he would stop cracking his knuckles or biting his finger nails

Heartburn Heartburn appears to be due to the regurgitation of gastric contents into an esophagus the mucosa of which has become sensitized in some way through emotion or the eating of some special food or the drinking of some special drink or the excessive smoking of some special type of tobacco or some cause hard to identify

The disease runs in some families it is common in Jews and the spells come and go often without discernible cause Anyone interested can consult a study I once made of the syndrome as seen in 123 patients The trouble is almost always functional" it is not necessarily associated with gastric hyperacidity and it is not due to peptic ulcer It cannot be helped by any operation Of the 574 relatives 5 per cent suffered from heartburn

Many of my patients with heartburn tell me that the essential point in the treatment is not to rely on swallowing an alkaline tablet Often this does not help What is much more likely to work is some sodium bicarbonate dissolved in half a glass of water This will wash the acid gastric juice out of the esophagus and with this, relief is likely to come

Regurgitation First, may I remind you that regurgitation is very different from vomiting the mechanism is simpler there is only reverse peristalsis in the stomach and esophagus without any contraction of the muscles of the abdominal wall The patient starts bringing up mouthfuls of food during or right after a meal The trouble is functional and I have never seen it corrected even by a half dozen operations In these cases there is no nausea Usually the patient is a young woman and often a mildly psychotic woman Of my 574 relative women 17 per cent or 1 in 6 were regurgitators Some were ruminators who swallowed again the food as it came up into their mouth I have seen rumination run through four generations of one family

The syndrome may be found in schizoid or in hysterical persons It is seen sometimes in young women suffering from anorexia nervosa they may regurgitate much of what little food they eat

The only treatment I know of for the syndrome is to ask the woman to try to hold the food down Some of the patients can do this but they hate to do it because it causes discomfort it is easier to let the stuff come up In those cases in which the girl is goofy or mentally retarded I do not attempt any treatment

Nervous vomiting In typical cases nervous vomiting is seen right after breakfast but not after luncheon or supper Neurotic soldiers sometimes upchuck their breakfast Among the 574 relatives 15 per cent told me of such vomiting One woman of 35 had been bringing up her breakfast for 17 years When I asked her if she had any psychotic relatives she said she surely had

I am sorry but I know of no good treatment for this disease

Nausea For much of my life I have wondered about the mode of production of nausea I have known that it is most likely to bother highly sensitive and neurotic and perhaps migrainous

persons especially when they are tired For instance a migrainous often tense dentist after a hard day in the office would wake about 2 a m and then suffer for two hours with nausea This distress would disappear the day he went on his vacation and would not come back until again he became overworked

It is possible that in many cases nausea arises in some part of the brain In other cases I suspect it is due to reverse ripples in the bowel as in cases of pregnancy where the tonus of the lower end of the bowel is markedly raised in some way perhaps by a spread of a fast metabolism from the rapidly growing uterus to the sigmoid segment of the colon

Certainly I have known patients who complained of nausea as the first symptom of a carcinoma growing in the highly sensitive sigmoid loop

I have been impressed by the fact that one practically never sees nausea produced by lesions high in the digestive tract—in the esophagus stomach duodenum gallbladder or pancreas It is interesting to note that 15 per cent of the 574 relatives told me of spells of nausea for which no abdominal cause had ever been found

Minor Distresses in the Cardia and Esophagus and Throat Due to Reverse Ripples I know of no good description in books of the many minor distresses which some persons feel in the region of the cardia and in the esophagus and pharnyx as ripples come gurgling up from the stomach into the throat Often such a gurgle will end in a burp " at which time the person may taste a bit of food that has been carried up from the stomach Sometimes these gurgles will run out the Eustachian tubes to the ears Sometimes they will produce hiccup and feelings of distress at the cardia The person may keep swallowing in an effort to drive the ripples down again Rarely an upcoming ripple will hit a swallowing wave going down the esophagus and this will cause a momentary rending pain

Perhaps the simplest way of getting these reverse ripples is to eat too big a dinner As every physiologist knows distention of some segment of a muscular tube will send off ripples or waves in both directions—orad and caudad

Another common way in which persons get these distressing

Many of my patients with heartburn tell me that the essential point in the treatment is not to rely on swallowing an alkaline tablet Often this does not help What is much more likely to work is some sodium bicarbonate dissolved in half a glass of water This will wash the acid gastric juice out of the esophagus and, with this relief is likely to come

Regurgitation First may I remind you that regurgitation is very different from vomiting the mechanism is simpler there is only reverse peristalsis in the stomach and esophagus without any contraction of the muscles of the abdominal wall The patient starts bringing up mouthfuls of food during or right after a meal The trouble is functional and I have never seen it corrected even by a half dozen operations In these cases, there is no nausea Usually the patient is a young woman and often a mildly psychotic woman Of my 574 relative women 17 per cent or 1 in 6 were regurgitators Some were ruminators who swallowed again the food as it came up into their mouth I have seen rumination run through four generations of one family

The syndrome may be found in schizoid or in hysterical persons It is seen sometimes in young women suffering from anorexia nervosa they may regurgitate much of what little food they eat

The only treatment I know of for the syndrome is to ask the woman to try to hold the food down Some of the patients can do this but they hate to do it because it causes discomfort it is easier to let the stuff come up In those cases in which the girl is goofy or mentally retarded I do not attempt any treatment

Nervous vomiting In typical cases nervous vomiting is seen right after breakfast but not after luncheon or supper Neurotic soldiers sometimes upchuck their breakfast Among the 574 relatives 15 per cent told me of such vomiting One woman of 35 had been bringing up her breakfast for 17 years When I asked her if she had any psychotic relatives she said she surely had

I am sorry but I know of no good treatment for this disease

Nausea For much of my life I have wondered about the mode of production of nausea I have known that it is most likely to bother highly sensitive and neurotic and perhaps migrainous

genologic facilities there at my disposal I could not find a cause for 9 in 10 of the recurrent spells of diarrhea complained of by many of my patients Then when I got to studying the 574 relatives" I found that 25 per cent or 1 in 4 complained of diarrhea —by which they usually meant short spells—perhaps consisting of 2 or 3 large movements These people had tried diets and medicines but nothing had helped On asking them what had happened just before a spell most said they did not know But perhaps after days or weeks when I succeeded in making friends with them most of these people admitted that they had some insane relatives and that their brief spells of diarrhea had come when on feeling queer they had gone into a panic fearing that they too were about to lose their minds

Some of them had a type of diarrhea with gas which on many a morning about 6 a m would force them out of bed Other "relatives had a daily and perhaps life long type of diarrhea that I could help only by giving codeine Some of these patients have been taking codeine now for 15 or 20 years without showing any tendency to run up the dose With codeine they can work and go about without it they would be chained to their homes and a toilet

Naturally in all these cases I rule out amebiasis by examining stools and by giving at one time 6 capsules of Carbarsone® I also rule out food allergy

Mucous Colics The commonest trouble at the lower end of the gut is the mucous colic I fear that many writers of books have lumped together several syndromes under this term Since I have suffered from mucous colics all of my long life I think I will confine myself to a description of the syndrome as I know it well In my case the syndrome is of hereditary and purely nervous origin The usual triggering cause has been nervous tension due to going out to dinner or having to attend some social function This is strange because I like people I meet them easily I am not self conscious I have no inferiority complex and I cannot imagine why an evening out should so stir up the nerves to my colon Also I cannot explain why a mucous colic may come when I am dining

reverse ripples is by getting constipated Then the distension of the lower end of the colon with a plug of feces will send off the ripples How do I know this? Because a few hundred times in my life when I have been much distressed by the reverse ripples in my esophagus I have suddenly remembered that an emergency phone call at breakfast had caused me to leave home without my usual bowel movement Then I have taken an enema and the minute the plug was removed from my rectum and sigmoid flexure the reverse ripples stopped and I was perfectly comfortable and unconscious of the fact that I had a digestive tract.

Sometimes with these reverse ripples due to constipation I have had much flatulence and some abdominal pain all of which also ended instantly with the taking of the enema

Constipation As I have just said within perhaps 9 hours after getting constipated a highly sensitive and reactive person can begin to suffer from a number of distressing symptoms such as abdominal pain much flatus and reverse ripples with belching and a tendency to hiccup—due apparently to the breaking of reverse ripples against the hiatus in the diaphragm Apparently the action current of a reverse ripple reaching the cardia stimulates electrically the muscle of the diaphragm As I have said all these symptoms disappear the minute the plug of feces is removed from the rectum and sigmoid flexure either by a natural bowel movement or an enema

It is useless for a comparatively insensitive person to tell me that I must be mistaken about these observations because he can go without a bowel movement for three days or even a week without the slightest discomfort I too can tell of people I have known who went comfortable without a bowel movement for a week or ten days at a time No—to tell a highly sensitive woman that she does not experience the symptoms here described is like telling a human barometer that she cannot sense in her aching joints a storm coming toward her several hundred miles away

Nervous Diarrhea During my 25 years at the Mayo Clinic I learned that even with all the excellent laboratory and roent

genologic facilities there at my disposal I could not find a cause for 9 in 10 of the recurrent spells of diarrhea complained of by many of my patients Then when I got to studying the 574 relatives I found that 25 per cent or 1 in 4 complained of "diarrhea —by which they usually meant short spells—perhaps consisting of 2 or 3 large movements These people had tried diets and medicines but nothing had helped On asking them what had happened just before a spell most said they did not know But perhaps after days or weeks when I succeeded in making friends with them most of these people admitted that they had some insane relatives and that their brief spells of diarrhea had come when on feeling queer they had gone into a panic fearing that they too were about to lose their minds

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happily with an old friend and may not come when I am giving the after banquet address before a big ball room full of people! Usually the syndrome becomes distressing after I have been at a big convention for several days

In my case constipation cannot be blamed because only rarely do I ever get a day of constipation I cannot blame food allergy I am tremendously sensitive to chicken, but when occasionally, I eat some chicken fat hidden in some dish, the syndrome that results is not at all that of a mucous colic

In some of my patients a mucous colic like mine comes with anxiety like that over an impending divorce or a business failure and in some cases a typical mucous colic follows sexual intercourse One can easily see how a spinal cord much stimulated by an orgasm might send out a nervous storm" to the pelvic colon I remember a nervous young man who passed a large mucous cast of the inside of his colon after spending three days in the company of a very amorous young woman In my own case a syndrome something like that of a mucous colic comes sometimes during the prodromal stage of a cold

My mucous colics start with the formation of gas in the bowel This I feel sure is excreted from the blood vessels into the colon With the resultant distension of the gut peristalsis becomes violent and waves that normally stop in the upper end of the rectum come right down to the anal ring where they cause much distress As some women with this syndrome say so well their bowel "starts yelling at them Then with the violent efforts of the lower colon to empty itself more gas forms together with some glairy fluid If the gas is quickly passed so that hyperperistalsis does not result the glairy fluid may not form but sometimes it forms without the hyperperistalsis

In a true mucous colic there is no passage of feces and this is a helpful diagnostic point For 2 or 3 days spasm in the left half of the colon will hold the feces back in the cecum The emptiness of the left colon can be shown with the help of an enema The water will come back clear

In my case this spasm of the descending colon about which we physicians talk and write so much never causes either pain or

discomfort. Whatever pain I ever have in a mucous colic is due purely to the strong efforts of the lower end of the bowel to empty itself When as often happens a mucous colic starts *an hour before* I have to go out to dinner while I am still at home and can go to the toilet every 20 minutes the syndrome is more or less aborted because the bowel does not remain full of the gas which would stir up peristalsis and the formation of mucus

In my case a mucous colic usually ends soon after I return home from an evening out As soon as all the gas is passed the bowel quiets down and no more mucus and gas are formed

I got a history of mucous colics in 7 per cent of the 574 "relatives" In my experience treatment with antispasmodics is illogical because the primary difficulty is not spasm of the colon but excess gas formation and the resultant hyperperistalsis The ideal remedy would be one that would stop the formation of gas Treatment with diet for a pure neurosis is also illogical In my case and in the case of hundreds of my patients the ideal and almost specific treatment has been codeine and papaverine of each ¼ of a grain If before going out for an evening—especially when from unconscious anticipation I start having the gas and hyperperistalsis—all I need do is to take one or two capsules of the codeine and papaverine and I am likely to remain comfortable all evening Especially for the young woman who fills up with gas and mucus when she goes out with a beau and then suffers terribly this treatment is often miraculously efficient

In consultation I have seen many a woman with supposed diarrhea who didn t have diarrhea—because she passed no feces She had only mucous colics In three typical cases the woman s husband was asking for a divorce and that was the trouble

Excessive Flatus In a normal person the gas which is constantly forming in the bowel is constantly being picked up by the blood, carried to the lungs and there excreted In some sensitive persons this process is reversed by anxiety and nervousness One can see this happen in cases in which a nervous man has catheters passed up through his ureters The first scout film will show no gas in the small bowel but the second film made after the catheterization may show the whole bowel filled with gas As I said

before in the cases of highly sensitive persons the presence of feces stagnating in the lower end of the colon can cause the continual excretion of gas into the bowel

Among the 574 relatives 12 per cent complained of much flatus

Hysterical Bloating Whenever a nervous woman complains of abdominal bloating which comes up during the day and goes down at night *without the passage of flatus* the physician must suspect the presence of the fairly common hysterical syndrome which I once described - He should have a scout film made of the distended abdomen because the absence of gas is diagnostic

A few of these women have so much pain that they get operated on half a dozen times others have no pain A surgeon need never be deceived into operating on one of these bloaters because when an anesthetic is started her abdomen will instantly go flat It is a remarkable fact that of the women relatives 37 per cent described this non gassy type of bloating due to a contraction of some of the muscles at the back of the abdominal wall

I am sorry to say that I know of no good treatment for these women Morphine makes them happy but it must not be given them because they can so soon get a habit In my experience diet, sedatives and anti spasmodics have no effect

Vague Types of Abdominal Distress and Indigestion It interested me much to note that 12 per cent of the 574 "relatives complained of vague indigestion and 8 per cent complained of abdominal distress and perhaps pain Seven per cent for years had suffered from the type of hunger pain which is not due to any ulcer

All embryo gastroenterologists and surgeons should be taught again and again that among the commoner symptoms complained of by persons going insane are abdominal pains and discomforts I have seen women who lost their severe abdominal pain the day a few electroshock treatments brought an end to the psychotic depression

Every physician should know that any abdominal pain or distress that is not influenced by eating or passing gas or feces is not

likely to be due to any lesion in the digestive tube All miseries that are widespread over the abdomen all long lasting pains and distresses and burnings and throbbings and butterflies are functional I have never seen them relieved by any operation

Gastric Crisis Types of Pain Some persons with migraine or epilepsy or a mild psychosis suffer from repeated episodic spells of severe abdominal pain of a gastric crisis type—often with violent retching A surgeon should never explore the abdomen of such a person when he learns that the woman has had many such spells before and always has gotten well in a day or two also when he notes that immediately on going into a spell the woman becomes lethargic and apathetic as in a bad attack of migraine also when he notes that the abdomen is unusually soft and the pulse and temperature and leucocyte count are normal and also when he asks and learns that just before each spell the woman has pain in or around one eye—pain which spreads back over one side of her head This of course means that the cause is migraine In other cases all the surgeon needs do to diagnose an epileptic equivalent is to ask and learn of forebears with epilepsy or a violent temper Then an EEG may show a typical dysrhythmia and the giving of Dilantin® may give relief In other cases it will be found that the patient is the highly neurotic or hysterical or poorly adjusted daughter of an insane mother or father

Migraine Hundreds of thousands of persons with atypical migraine fail to get the correct diagnosis At the Mayo Clinic about 20 per cent of the persons I saw with a weird abdominal syndrome had a previously unrecognized migraine Many such persons I could relieve with the help of ergotamine preferably injected intramuscularly the minute an attack started

Very important is the fact that most of the patients I saw with a violent or atypical migraine perhaps with severe abdominal pain had migraine inherited from one ancestor plus epilepsy or a psychosis inherited from the other side of the family "Migraine plus something" is a diagnosis which should be made much more often than it now is

A high percentage of migrainous women suffer from a "func

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learned that the woman's scalp and face on her right side were so sensitive that she could hardly stand washing her hair or her face

Anorexia Nervosa Any physician of any experience should be able to make the diagnosis of anorexia nervosa the minute he sees a young woman who does not seem to be much concerned over the fact that she has gone down in weight to perhaps 79 pounds She is eating almost nothing and perhaps regurgitating much of that The point I would emphasize is that, too commonly today the physician in charge fails to realize that he is dealing with a mildly psychotic patient often a schizophrenic and usually a member of a psychotic family Because of the bad nervous heredity of these women they are likely to slump again after they have been fattened and apparently cured

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tional pain in the right upper quadrant of the abdomen This is never relieved permanently by the removal of the gallbladder—even when it contains stones

Little Strokes In the cases of all persons past middle age who suddenly get abdominal pain, perhaps with nausea and vomiting dizziness and mental confusion from which they do not easily recover the physician must think of a little stroke I see many of these persons Some suddenly lose 50 pounds and then their weight stabilizes for the next several years

Food Allergy In the cases of young persons with spells of puzzling abdominal pain or discomfort with foul gas and perhaps some diarrhea or rarely an anaphylactic type of shock the physician must think of food allergy Perhaps then the keeping of a diary of *unusual* foods eaten just before a spell will show what the offending substance it

Fibrositis or Arthritis Occasionally I see persons whose abdominal discomfort is obviously due to a fibrositis in the abdominal wall or to an arthritis in the spine or in the joint between the lower end of the sternum and the xyphoid appendix or in the two little joints at the ends of the tenth ribs In some cases one can show that the distress is in the abdominal wall and not in the abdomen by just picking up a fold of the abdominal skin and fat and pinching it If the woman then flinches and screams with pain it will be obvious where her hypersensitiveness is it is not deep in her abdomen

Thalamic Syndrome In a few of the patients I see who for years because of a pain in one loin have been puzzled over especially by urologists I find a typical thalamic syndrome In taking the history no assistant had ever brought out the fact that the woman had severe distress not only in one side of the abdomen but in *all of that side* of her body from her scalp and face to her toes I remember a woman like this who had had two futile operations for a supposed ruptured disc and then two futile operations for the splinting of her spine and one sacro iliac joint None of this work would ever have been done if the surgeons had

stomach pouch The symptoms are not unlike those experienced by persons with intact stomachs after they have eaten an unusually large meal Thus *they have a feeling of bloating fullness* distention nausea and generalized epigastric discomfort Regurgitation and vomiting frequently occur immediately after a meal Although the symptoms are fairly characteristic it is well to have a roentgenographic examination to confirm the assumption that the remnant of the stomach is small and to note whether the occurrence of symptoms is coincident with distention of the gastric pouch The treatment consists of small frequent feedings and *patience since in most cases the size of the pouch increases* or at least tolerance to the presence of larger quantities of food at a given time is developed

The oral use of local anesthetics such as 15 cc of 6% procaine in methyl cellulose or 2% Xylocaine® viscous taken immediately before meals may help prevent symptoms temporarily

Stomal Obstruction This is usually caused by surgical creation of a stoma which is too small It may also result from stenosis secondary to a recurrent marginal ulcer The symptoms are characteristic and consist of vomiting undigested food which is not bile stained soon after eating The diagnosis is confirmed by roentgenographic examination as well as by direct visualization of the stenotic stoma with a gastroscope The treatment for this condition is surgical revision of the stoma

Afferent Loop Obstruction This is an untoward surgical complication of the Billroth II operation It results from adhesions volvulus or herniation of the afferent loop under the efferent limb The symptoms may be sudden severe and acute as in any acute intestinal obstruction A hyperactive bowel segment may be seen as well as palpated Immediate surgery to correct this condition is necessary In some cases there are chronic symptoms which may or may not be severe such as hyperperistalsis and nausea vomiting and distention occurring soon after meals Roentgenographic examination usually confirms the diagnosis of obstruction in these cases Further surgery is necessary

Efferent Loop Obstruction This is another untoward surgical

POSTGASTRECTOMY SYNDROMES

J Alfred Rider M D Ph D *

GASTRIC resection produces changes from the normal physiological state which in turn may cause disturbances in motility Many of the symptoms from which a patient may suffer when part of his stomach has been removed are produced by these resulting motility disturbances However postgastrectomy syndromes in this discussion will include all signs and symptoms caused by partial gastric resection Since total gastric resection is much less common than partial gastric resection, problems resulting from total gastrectomy even though they are more complex will not be included

Postgastrectomy syndromes will be discussed under the following five headings

1 Mechanical disturbances
2 Recurrent ulcerations
3 Psychological disturbances
4 Physiological problems
5 Gastritis

MECHANICAL DISTURBANCES

In a recent symposium Jordan[40] discussed the following mechanical problems

The Small Stomach Syndrome When 50% or more of the stomach has been removed the patient may suffer symptoms which are directly caused by rapid overdistention of a small

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For patients who do not respond to a strict ulcer regimen and for those who have recurrences there is the choice of x ray therapy or further surgery X ray therapy is especially valuable for those who are poor surgical risks and for those in whom the contemplated surgery is a high subtotal or total gastric resection [64] The usual x ray treatment consists of giving a patient approximately 1500 r to the stomach within a 10 12 day period The treatment fields are rectangular in shape usually 10x15 cm The radiation field covers the entire stomach from the cardia to the incisura The treatment ports are checked by examining roentgenographic films after the patient has swallowed a barium sulfate suspension

The dose is delivered by 250 kvp x ray with a half value layer of 2 8 mm of copper and a target skin distance of 50 cm Rarely a patient experiences minor side effects consisting of nausea from this treatment

The rationale of this treatment is the expectation of reducing or abolishing gastric acidity since there is always complete healing in patients with achlorhydria The ulcers will remain healed as long as the patient is achlorhydric and frequently even when acidity returns

A vagotomy is the surgical treatment of choice for patients who have already undergone gastric resection

Recently much attention has been paid to non beta cell islet pancreatic adenomas it is important to be aware of the possibility of this disease in all patients who have recurrent resistant ulcers associated with high gastric acidity Treatment in this case is surgical resection of the pancreatic adenomas

PSYCHOLOGICAL DISTURBANCES

It has often been suggested that many patients who have symptoms after gastric surgery are psychoneurotic If this is true the symptoms are not caused by the surgery but it may be that those who require this type of surgery are likely to have had previously existing psychiatric difficulties For example those who lose weight after surgery are usually thin and nervous to begin with The recent works of Leonard Papermaster and Wangensteen[61] have shown that hypnosis is effective in relieving postgastrectomy

complication and may be either low grade or high grade with corresponding symptoms It may be produced by volvulus obstruction caused by adhesions herniation of the efferent loop under the afferent limb or jejunogastric intussusception If the obstruction is high grade or acute immediate surgery may be necessary as in the case of any intestinal obstruction Usually however it is not complete or acute, but is chronic If it is chronic it is characterized by nausea and vomiting of bile stained retained food and secretions soon after eating When the diagnosis is confirmed by roentgenographic examination surgical intervention is necessary

RECURRENT ULCERATION

Approximately 5% of all patients who have partial gastric resection because of peptic ulcer develop a stomal a marginal or a jejunal ulcer This recurrent ulceration occurs much more frequently after surgery for a duodenal ulcer and is more common after a Billroth I operation than after the Billroth II operation It is more likely to occur in patients who secrete a large amount of acid The symptoms are similar to those of gastric or duodenal ulcer and frequently consist of postprandial burning or epigastric distress they may however occur a little sooner following meals after surgery than before surgery

Diagnosis is made by roentgenographic examination as well as by gastroscopy but it is frequently easier to demonstrate an ulcer on the gastric side of the stoma with the use of the gastroscope than with the roentgenographic technique

Treatment is medically much more difficult than for either a duodenal or a gastric ulcer This is largely because antacids do not stay in the stomach very long Within a matter of a few minutes an antacid is washed out of the stomach and the acid gastric juice which follows it continues to bathe the new ulcer However following frequent ingestion of antacids—at least every ½ hour—in adequate amounts or a continuous drip of milk or milk and antacid most of these ulcers will heal Anticholinergic drugs such as Pamine® 2.5 to 5 mg four times a day before meals as tolerated are of benefit It is also necessary that the patient follow a diet for ulcer

with peptic ulcer and that further changes take place following gastric resection *He felt that a study of adrenal functions might* help elucidate the mechanisms of post gastrectomy hypoglycemia This is an interesting possibility but for practical purposes the treatment at present is similar to that for functional hypoglycemia and consists of frequent high protein feedings anticholinergic drugs and mild sedation

Dumping Syndrome The term dumping as it is now known was probably first used by Mix[48] in 1922 to describe a pooling of barium in the small bowel following gastroenterostomy Recently Machella[44] has excellently summarized the salient features of the dumping syndrome It is now generally accepted as the term which applies to a complex set of symptoms occurring almost im mediately after the entrance of food or electrolytes into the jejunum

The symptoms may consist of pain in the epigastrium nausea a bloated or full feeling belching vomiting of bile explosive diar rhea and vomiting of food Frequent vasomotor components of this syndrome are a feeling of warmth weakness perspiration palpitation, dizziness pallor chilliness tachycardia drowsiness and collapse with loss of consciousness These symptoms vary greatly in severity and degree and are lessened or abolished by lying down immediately after meals They usually disappear in 30 to 60 minutes Symptoms are more likely to occur after a large meal and concentrated carbohydrates seem to be more likely than other foods to cause difficulty Since some patients volun tarily decrease their food intake they may subsequently develop malnutrition with hypoproteinemia edema and multiple vitamin deficiencies

Although statements regarding the incidence of the dumping syndrome differ in various studies it has been found to occur in as many as 80 per cent of a series of gastrectomy patients It may follow any type of gastric surgery such as Billroth I and Billroth II gastrectomies gastroenterostomy pyloroplasty vagotomy and segmental gastric resection although it is probably less likely to occur after a Billroth I procedure than after any of the other operations

symptoms In our experience however it appears that psycho neurotic postgastrectomy patients are in the minority

PHYSIOLOGICAL PROBLEMS

Postgastrectomy problems which are predominantly physiologi cal in origin may best be discussed in terms of the following three syndromes

Malabsorption Syndrome A significant failure of absorption primarily of fat but also of iron, vitamins and proteins occurs in some patients The exact cause of this failure is unknown but it may be related to hypermotility or dissociation of pancreatic juices and bile from ingested food or both The treatment is com plex and must be devised individually for each patient In addi tion to a low fat diet Panteric® granules or Viokase® may be given with each feeding However in the case of a patient who is severely ill it may be necessary to prescribe two capsules or 1 tea spoon of Panteric® granules or Viokase® hourly If these measures do not suffice to effect improvement it may be necessary to re strict the intake of fat considerably Supplemental iron and vita mins including vitamin B_{12} administered parenterally are often of great benefit In some of our studies we have found that the absorption of food is increased in some of these patients if they take alcohol with each meal In addition to increasing absorption the alcohol may have an appetite stimulating effect so that there is an increase in the intake of calories Although my experience with Nilevar® is limited I have been favorably impressed by the amount of weight gained by some patients taking 10 mg three times a day

Hypoglycemia Syndrome or Late Postgastrectomy Syndrome Symptoms are typical of hypoglycemia and occur 2 to 4 hours after meals The diagnosis is made on the basis of characteristic symptoms of weakness syncope cold perspiration restlessness nervousness tachycardia hypotension and in rare cases convul sions The cause is probably related in some way to hypermotility However Pare [illegible] in a study of 122 patients who had undergone gastric resection because of peptic ulcer concluded that " there is an abnormality of carbohydrate metabolism in patients

as well as tachycardia and changes in the blood pressure Significant decreases in plasma potassium and phosphate as well as an increase in the excretion of sodium chloride and uric acid have been noted

Machella[44] concludes, that the reaction is set off by distention of a segment of small intestine by fluid which passes into the gut lumen from the blood stream in an attempt to reduce the osmotic properties of certain ingested foodstuffs Some of the systemic changes which accompany the reaction are similar to those which follow the administration of cholinergic and adrenergic drugs suggesting a reflex stimulation of both the sympathetic and parasympathetic divisions of the autonomic nervous system Other changes depend on the chemical nature of the material producing the reaction

Peddie Jordan and DeBakey[54] found a decrease in postprandial plasma volume averaging 420 cc in 14 of 16 symptomatic patients whereas there was an average decrease of 92 cc in 5 of 15 asymptomatic patients Smith[7 7] reported changes in electrocardiograms which suggested hypopotassemia and Peddie *et al* and other authors have shown a postprandial fall in serum potassium However in Peddie s series there was only an average fall of 0 88 mEq /L in the asymptomatic patients and 0 97 mEq /L in the symptomatic patients

Medwid *et al* [4?] gave further support to the concept that change in volume is a cause by showing that when 500 ml of a plasma expander were given intravenously at the time the dumping syndrome was expected to occur the symptoms were effectively prevented

Patients with the dumping syndrome generally respond to medical treatment. Symptoms can be ameliorated or abolished by avoiding foods and agents which form hypertonic solutions namely sugars and electrolytes Frequent small feedings of foods with a low total osmotic activity that is high in protein moderate in fat and low in starches are very important Fluids should not be taken during meals It is frequently necessary to instruct a patient to lie down for half an hour to an hour after eating Anticholinergic drugs in large amounts such as Pamine® 5 mg plus

Many studies have been made in attempts to elucidate the mechanisms of the dumping syndrome Machella[44] has carefully outlined many of them For example it has been found that this symptom complex can be produced by a variety of foodstuffs and electrolytes However the ingestion of substances lacking high osmotic pressure does not produce these symptoms It is even possible to produce these symptoms in normal patients by instilling hypertonic solutions into the jejunum Motility studies have indicated that an increase in intraluminal pressure and motor activity of the small bowel are part of the dumping syndrome Severe symptoms may be produced by distending the small bowel or preventing the passage of food or intestinal content through it by means of an obstructing balloon Symptoms can be lessened or prevented if the patient assumes a recumbent position immediately after eating and they may be stopped promptly by vomiting or evacuating the bowel Nervous tension aggravates the symptoms

Symptoms and signs of the dumping syndrome vary considerably in different patients both in severity and in the types which predominate Numerous theories as to the cause have been propounded Gastritis hypoglycemia hyperglycemia hypermotility of the bowel distention and increased intraluminal pressure of the small bowel caused by ingested food stretching of the gastric remnant, reflux of food into the afferent loop changes in plasma volume changes in serum potassium achlorhydria dissociation of the ingested food and pancreatic enzymes and bile impaired blood supply to the brain due to abnormal blood perfusion of the viscera following a meal and a strong psychic element all have been postulated

Some of these theories have been supported by experimental studies the following are some examples When hypertonic glucose is introduced directly into the small bowel it apparently tends to become isotonic by withdrawing fluid from the blood stream with a resultant decrease in the volume of circulating blood Temporary hyperglycemia with glycosuria and increased motor activity occur after an increase in intraluminal pressure in the jejunum Electrocardiographic changes have been reported

as well as tachycardia and changes in the blood pressure Significant decreases in plasma potassium and phosphate as well as an increase in the excretion of sodium chloride and uric acid have been noted.

Machella[44] concludes that the reaction is set off by distention of a segment of small intestine by fluid which passes into the gut lumen from the blood stream in an attempt to reduce the osmotic properties of certain ingested foodstuffs Some of the systemic changes which accompany the reaction are similar to those which follow the administration of cholinergic and adrenergic drugs suggesting a reflex stimulation of both the sympathetic and parasympathetic divisions of the autonomic nervous system Other changes depend on the chemical nature of the material producing the reaction

Peddie Jordan and DeBakey[54] found a decrease in postprandial plasma volume averaging 420 cc in 14 of 16 symptomatic patients whereas there was an average decrease of 92 cc in 5 of 15 asymptomatic patients Smith [7] reported changes in electrocardiograms which suggested hypopotassemia, and Peddie *et al* and other authors have shown a postprandial fall in serum potassium However in Peddie s series there was only an average fall of 0 88 mEq /L in the asymptomatic patients and 0 97 mEq /L in the symptomatic patients

Medwid *et al* [3] gave further support to the concept that change in volume is a cause by showing that when 500 ml of a plasma expander were given intravenously at the time the dumping syndrome was expected to occur the symptoms were effectively prevented

Patients with the dumping syndrome generally respond to medical treatment. Symptoms can be ameliorated or abolished by avoiding foods and agents which form hypertonic solutions namely sugars and electrolytes Frequent small feedings of foods with a low total osmotic activity that is high in protein moderate in fat and low in starches are very important Fluids should not be taken during meals It is frequently necessary to instruct a patient to lie down for half an hour to an hour after eating Anticholinergic drugs in large amounts such as Pamine® 5 mg plus

a sedative such as phenobarbital or a tranquilizer will frequently give additional benefit when taken before meals

Recently Robinson and Pittman[68] have elaborated a series of diets for dumping syndrome patients based on the assumption that if the type and volume of food is increased gradually in a prescribed manner symptoms will largely be prevented My experience is that it is usually not necessary to be so strict in the matter of diet strict diet is however important for the patient with severe symptoms Fortunately there are not many patients with severe symptoms If the physician perseveres almost all patients with the dumping syndrome can be rehabilitated Only rarely is it necessary surgically to substitute a reconstructed gastric pouch

GASTRITIS

In order to evaluate the role of gastritis in the symptomatology of postgastrectomy syndromes 68 patients 45 males and 23 females whose ages ranged from 27 to 77 years were examined gastroscopically The majority had undergone gastric surgery for duodenal or gastric ulcer and had developed persistent postoperative symptoms such as postprandial nausea and vomiting dysphagia diarrhea weakness hemorrhage or anemia Thirty three of the patients had no evidence of gastritis and 35 had evidence of the following types of gastritis 9 were atrophic 9 hypertrophic 12 were superficial and 5 were of a mixed type Table I and Table II show the occurrence of various symptoms in these patienth with and without gastritis It is clear that there is no symptom which is specifically characteristic of any form of gastritis and that the symptoms in these patients do not appear to be unusual Furthermore there does not seem to be any quantitative or qualitative difference between those with gastritis and those who do not have gastritis This does not necessarily mean however that gastritis is unimportant in the symptomatology of the postgastrectomy syndrome It does indicate that it cannot be considered to be the only factor It is my feeling that gastritis is simply an additional complication of surgery and probably results from the irritating effects of the reflux of bile or pancreatic enzymes or both into the gastric pouch It is always possible how

TABLE I

Postoperative Patients	68
Subtotal gastrectomy	54
Gastroenterostomy without gastric resection	14
Negative gastroscopy	33
Gastritis	35
Hypertrophic	9
Atrophic	9
Superficial	12
Combined	5

TABLE II

Symptoms Occurring in 35 Patients with Gastritis

Symptom	*Instances*
Persistent vomiting	12
Epigastric pain	20
Gas bloating	3
Nausea	8
Massive bleeding	8
Heartburn	1
Regurgitation	1
Postprandial sweating	1
Weakness	3
Diarrhea	1
Dysphagia	1
Severe weight loss	2
Anemia (without gross bleeding)	3

Symptoms Occurring in 33 Patients without Gastritis

Symptom	*Instances*
Persistent vomiting	13
Epigastric pain	25
Gas bloating	7
Nausea	13
Massive bleeding	8
Heartburn	5
Regurgitation	2
Postprandial sweating	3
Weakness	3
Diarrhea	3
Severe weight loss	1
Anemia (without gross bleeding)	2

ever that gastritis existed prior to surgery or that its occurrence after surgery was merely coincidental.

I have prescribed vitamin B_1 1000 mcg. at weekly intervals for 6-8 weeks on an empirical basis and patients have reported some benefit from this therapy.

Additional treatment should be prescription consisting of a

bland ulcer type diet and mild sedatives or tranquilizers and anticholinergics A number of patients seem to respond well to antacid therapy even though their gastric acidity may be low or absent Antacid therapy may be effective in this latter group because the mucosa of patients who have gastritis is irritated very easily especially by acid foods If antacids are used they should be used in adequate amounts and at intervals of one to two hours Finally it has been found that 4 to 15cc of 2% Xylocaine® viscous may be very effective in relieving or preventing symptoms when given before or after meals or both

SUMMARY AND CONCLUSIONS

The various kinds of postgastrectomy syndromes have been discussed Some of these are amenable to surgery, others are benefited by a strict medical management With perseverance and individualization of therapy the great majority of patients with postgastrectomy syndromes can be completely rehabilitated Special treatment must be devised for the occasional patient who presents an unusual problem

The incidence and various types of protracted morbidity seen following gastric surgery indicate the importance of careful evaluation and good conservative medical management of all peptic ulcer patients before a surgical procedure is contemplated

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THE PATHOGENESIS AND TREATMENT OF ACUTE DILATATION OF THE STOMACH AND PARALYTIC ILEUS

LESTER R DRAGSTEDT MD PH D *

UNDER normal conditions the gastric and pancreatic secretions poured into the upper part of the alimentary tract are more or less completely absorbed in the intestines lower down Water and inorganic salts the principal constituents of these secretions are not appreciably absorbed in the stomach duodenum or even upper jejunum A given quantity of water or salt solution placed in an isolated portion of this part of of the digestive tube may be recovered quantitatively several hours later In the lower jejunum ileum and colon however the absorption of water and certain inorganic salts may be readily demonstrated by this method It is thus clear that for reabsorption the gastric and pancreatic juice must be carried by the motor activities of the intestine into the ileum and colon Interference with this transport or failure of absorption after reaching the lower bowel must result in the loss of the various constituents of these secretions to the body either through vomiting accumulation in the lumen of the non absorbing portions of the tract diarrhea or escape through a fistulous opening

The conception that harm might result from the failure of re

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* Professor of Surgery The University of Chicago (The experimental work on which this paper is based has been aided by grants from the Otho S A Sprague Memorial Institute and the Division of Research Grants and Fellowships of the National Institutes of Health United States Public Health Service)

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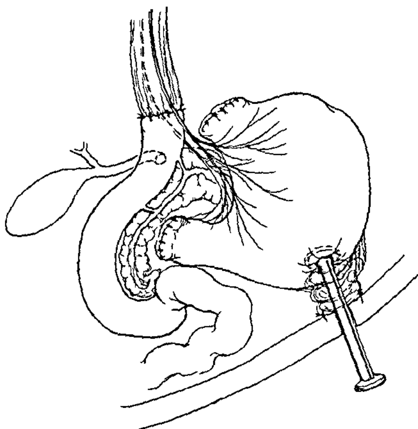


Fig 1 Diagram illustrating the vagus innervated total stomach pouch prepared by Dragstedt and Ellis The continued loss of gastric juice from such a pouch produces progressive dehydration de mineralization and ultimately death unless compensated for by the parenteral administration of salt solution

volume of gastric juice lost was sufficient to prevent the changes in the blood chemistry and to preserve the lives of these animals for long periods of time

The pancreas has the same capacity to separate the water and inorganic salts from the plasma and animals provided with an adequate total pancreatic fistula secrete themselves to death This fact was first demonstrated by Elman and McCaughan[4] and

absorption of gastric and pancreatic juice came about largely through experimental work on the pathogenesis of high intestinal obstruction. While Hartwell and Hoguet[1] were the first to point out the significance of dehydration in this condition, it was the classical work of Gamble and his associates that established the importance of the electrolytes in the gastrointestinal secretions and especially the sodium ion in enabling the body to retain water. The loss of gastric juice was offered as an explanation for the hypochloremia, alkalosis and dehydration that accompany obstruction at the pylorus. Such a theory necessarily assumed that the gastric glands and the pancreas can separate the elements for their respective secretions from the blood plasma when these elements are reduced below their *normal concentration*. It furthermore assumed that these glands can continue this separation of essential constituents from the altered blood plasma until the latter becomes so abnormal that life cannot further exist. The mechanism for maintaining a constant composition of the blood upon which life depends would then seem to be subordinate to the mechanism for manufacturing a digestive juice. That this idea is correct, however, was demonstrated by Dragstedt and Ellis when they first prepared vagus innervated isolated stomach *pouches in dogs*.[3] These animals were found to secrete large volumes of highly acid gastric juice from the isolated stomach. There was no element of obstruction present, food passing readily from the esophagus into the duodenum (fig. 1). Even though supplied with food and water, these animals rapidly lost weight and strength and usually died within two weeks. Accompanying the deterioration in their physical state was a profound alteration in the chemistry of the blood. There was a profound fall in the concentration of blood chloride, an increase in the carbon dioxide combining power of the plasma, a shift in the pH toward the alkaline side, and a late increase in non-protein and urea nitrogen. The changes in the blood chemistry were roughly proportionate to the severity of the symptoms and both were without question due to the secretion and failure of reabsorption of the gastric juice. The daily parenteral administration of physiological salt solution or Ringer's solution in amounts roughly equivalent to the

stomach and paralytic ileus following surgical trauma or in generalized acute peritonitis It is not within the scope of this paper to attempt any comprehensive survey of the clinical and experimental data and resulting conceptions regarding the etiology and pathogenesis of acute dilatation of the stomach In a previous publication[1] I have offered the following interpretation of the etiological factors in this distressing complication of surgical treatment During the course of the operation there occurs a profound stimulation of either visceral or somatic sensory nerves depending upon whether the operation is intra or extra abdominal This produces a profound reflex inhibition of the tonus and motility of the stomach as a result of which it becomes greatly distended by swallowed air and the accumulating secretions of the gastric mucosa (figs 2 3 4 and 5) In many cases although apparently not in all the dilated stomach forces the intestines into the pelvis and produces a secondary compression of the inferior horizontal portion of the duodenum by the fold of mesentery containing the superior mesenteric vessels When this occurs even though the obstruction be relatively slight the atonic stomach and duodenum are unable to force their secretions into the lower intestine As a result they accumulate in the non absorbing dilated stomach and proximal duodenum and overflow into the mouth They are thus effectually lost to the body and as we have seen this removal of sodium and chloride ions by the stomach and pancreas is entirely adequate to account for the death that occurs in untreated cases with the well known preliminary dehydration and anuria

In acute generalized peritonitis likewise this failure of absorption of gastric and pancreatic juice must be considered as a major pathogenic factor That hypomotility to complete atony of the gastro-intestinal tract exists in this disease is of course well known It seems probable that this is partly due to the direct action of bacterial toxins on the intestinal wall but to a greater degree to reflex inhibition from the irritated and inflammed peritoneum It is easy to demonstrate such a visceral reflex in a cat under light ether anesthesia or after decerebration Stimulation of the parietal or visceral peritoneum by traction or electrical stimulation causes complete inhibition of the movement of the stomach and intes

by Dragstedt Montgomery Matthews and Ellis [illegible] As would be expected from the separation of an alkaline secretion from the blood the chemical alterations in the plasma were in some respects opposite to those following the continued loss of gastric juice Thus there occurred a reduction in the total plasma base, a decrease in the concentration of chloride a decrease in bicarbonate and a shift in the pH toward the acid side and again, a late increase in non protein and urea nitrogen Here again the symptoms were proportionate to the alterations in the blood chemistry and were due to the secretion and failure of reabsorption of the pancreatic juice The chemical alterations in the blood were prevented or restored and life preserved by the parenteral administration of physiological salt solution The importance of reabsorption of gastric and pancreatic juice and *especially* of the sodium and chloride ions of these secretions has thus been well established

It is accordingly very evident that the property of the gastric and pancreatic glands whereby they can remove inorganic elements from the blood plasma until death is produced makes it necessary that their secretions pass into the absorbing portions of the intestine and there be returned to the blood Under normal conditions of course this occurs It is likewise readily apparent that such factors as profuse persistent vomiting gastric or high intestinal fistulae or profuse diarrhea will prevent this reabsorption Patients with gastro colic fistulae occasionally display alterations in blood chemistry similar to those following obstruction at the pylorus When complete obstruction occurs in the upper small intestines gastric and pancreatic juice are lost because they cannot reach the absorbing bowel Even in low obstructions the reflex vomiting accompanying distention of the obstructed segment produces a loss of these secretions There is now no doubt that this failure of reabsorption of gastric and pancreatic juice is a very important factor in the pathogenesis of ileus and fortunately one that can now be adequately controlled

It is however in the following types of gastro-intestinal pathology that I wish to stress the role of failure of reabsorption of these digestive juices namely acute postoperative dilation of the

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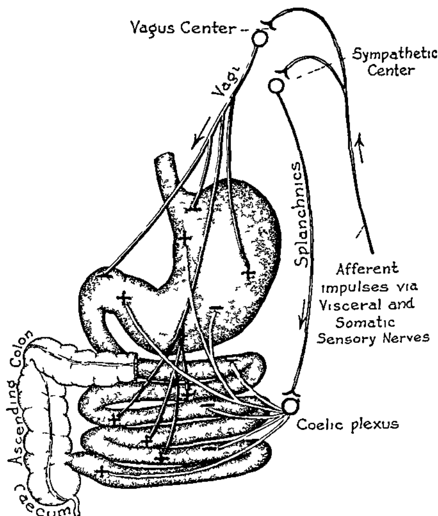


Fig 2 Diagram illustrating reflex inhibition of the motility of the stomach and intestines produced by stimulation of visceral or somatic sensory nerves The trauma of a surgical operation produces reflex inhibition of the vagus center and simultaneous stimulation of the sympathetic centers The relaxed stomach is dilated by swallowed air and accumulating gastrointestinal secretions In generalized peritonitis movements of the inflammed intestines stimulate visceral sensory nerves and produce reflex inhibition of gastrointestinal motility in a similar way

tines This is partly prevented by previous section of the splanchnics or by spinal anesthesia Gastric and pancreatic juice not



Figs 3 4 and 5 illustrate the enormous siz of the dilated stomach These figures were supplied by Dr William J Gillesby of Chicago An excellent article n acute gastric dilatation by William J Gillesby and James R Wheeler appeared in the *American Surgeon* 22 1154 1956 The patient illustrated in figure 3 was found to contain 4700 cc of fluid in the dilated stomach at autopsy



Fig 5

being propelled into the lower jejunum ileum and colon accumulate in the non absorbing stomach and duodenum and are lost by regurgitation or vomiting It is therefore not surprising to find

in acute peritonitis those changes in the blood chemistry which result from the simple uncomplicated loss of gastric and pancreatic juice The profound improvement produced by the administration of large quantities of physiological salt solution or Ringer's solution in these patients is an index of the significance of this factor in the pathogenesis of the disease

Acute dilatation of the stomach and paralytic ileus represent two post operative complications that have very largely disappeared as a result of a better understanding of their pathogenesis and the availability of adequate treatment However a real hazard lies in the fact that the absence or rare occurrence of these complications has led some of our younger surgeons to doubt their serious nature and to question the methods that have been developed both for prevention and cure This situation is not new and it may be helpful to recall how the discoveries of one generation have been forgotten by the next with disastrous consequences and have had to be rediscovered again

In 1832 Latta[7] wrote a paper entitled Treatment of Cholera by the Copious Injection of Aqueous and Saline Fluids into the Veins In 1855 John Snow[8] pointed out that the collapse in cholera patients the concentration of the blood the decreased secretion of urine and death are all due to the withdrawal of water and salt from the blood so that it assumes the thick tarry appearance so well known to all who have opened a vein in cholera A quotation from Snow may be of interest In all cases of cholera that I have attended the loss of fluid from the stomach and bowels has been sufficient to account for the collapse when the previous condition of the patient was taken into account together with the suddenness of the loss and the circumstance that the *process of absorption appears to be suspended*—*The stools* and vomitive matters in cholera consist of water containing a small quantity of the salts of the blood and a very little albuminous substance The change in the blood is precisely that which the loss by the alimentary canal ought to produce and indeed it is physically impossible that the alteration in the blood can be caused in any other way —The diminished volume of the blood causes many of the symptoms of a true hemorrhage as debility faintness and coldness while these effects are much increased by

its thick tenacious condition which impedes its passage through the pulmonary capillaries thereby reducing the contents of the arteries throughout the system to the smallest possible amount as indicated by the small thready pulse The interruption to the pulmonary circulation occasioned by the want of fluidity of the blood is the cause of the distressing feeling of want of breath — If any further proof were wanting than those above stated that all the symptoms attending cholera except those connected with the alimentary canal depend simply on the physical alteration of the blood and not on any cholera poison circulating in the system it would only be necessary to allude to the effects of a weak saline solution injected into the veins in the stage of collapse The shrunken skin becomes filled out and loses its coldness and lividity the countenance assumes a natural aspect the patient is able to sit up and for a time seems well If the symptoms were caused by a poison circulating in the blood and depressing the action of the heart, it is impossible that they should thus be suspended by an injection of warm water holding a little chloride of soda in solution

One of John B Murphy s great contributions to surgery was his practice of instilling physiological salt solution into the rectum and colon of patients suffering from generalized peritonitis or paralytic ileus The so called Murphy Drip was well known to the surgeons of the early decades of the twentieth century It was assumed by the surgeons who were my teachers in Chicago that the benefits claimed by Murphy were due to the water that was absorbed from the colon by these sick patients In one case disastrous results occurred when saturated salt solution was introduced by mistake into the colon instead of physiological salt solution As a result of this experience the use of salt solution and the Murphy Drip were prohibited and plain warm tap water substituted In a short time it was concluded that the rectal administration of tap water by Murphy s method had very little real beneficial effect and so was abandoned In subsequent years many people with paralytic ileus generalized peritonitis or acute dilatation of the stomach died from dehydration and demineralization before the studies of Gamble in the 1920 s securely established the value of the parenteral administration of salt solution

in patients losing the digestive secretions

A second factor that requires emphasis in a discussion of the pathogenesis of these diseases is overdistention of the alimentary tract and the subsequent effect that such overdistention produces on gastro-intestinal tonus and motility The trauma of surgery produces reflex inhibition of the tonus and motility of the stomach and intestines So also do reflexes from the inflamed peritoneum in patients with generalized peritonitis The inhibition thus produced is aggravated by the distending effect of swallowed air and the secretions of the digestive glands Overdistention of the stomach or the intestines produces paralysis of the smooth muscle in a manner similar to that resulting from overdistention of the urinary bladder or in acute dilatation of the heart Overdistention of the small intestines is the most reliable method for producing paralytic ileus in experimental animals I have been particularly impressed with the damaging effect of overdistention of the stomach as a result of my early experience in the treatment of duodenal ulcers by cutting the vagus nerves to the stomach Division of the vagus nerves to the stomach leaves unopposed the inhibitory effect of its sympathetic innervation Some time is required before the local automatism of the stomach permits it to resume normal gastric peristalsis If the stomach is permitted to become overdistended by swallowed air food or gastric secretions during the first three or four days after gastric vagotomy the gastric wall becomes paralyzed more as a result of overdistention of the smooth musculature in its wall than to the removal of its motor innervation A great deal more effort is required to get resumption in motility in such an overdistended stomach than is required if the distention is entirely prevented The loss of the motor effect of the vagus nerves is shortly compensated for and after a variable time the motor function of the vagotomized stomach is within normal limits

One of Owen Wangensteen s great contributions to surgery was his introduction and popularization of suction decompression of the stomach in surgical patients This simple procedure has completely changed the outlook in several of these common surgical complications When routinely adopted after major surgery it has prevented the appearance of acute dilatation of the stomach

Paralytic ileus as a surgical complication has likewise almost entirely disappeared Gastro intestinal decompression has proved to be an extremely important factor in the treatment of generalized peritonitis It goes without saying that the water and inorganic salts sucked out of the upper gastro-intestinal tract must be replaced by the parenteral administration of these substances

These matters that I have been discussing are not new but there is some danger that they may be forgotten or their significance underestimated Since acute dilatation of the stomach and paralytic ileus have become rare there is danger that the possibility of their development may be underestimated Naso gastric suction has some obvious disadvantages it is uncomfortable it interferes somewhat with the expulsion of mucus from the respiratory tract and if used for a long period of time may cause actual necrosis in the larynx This has caused some surgeons to abandon

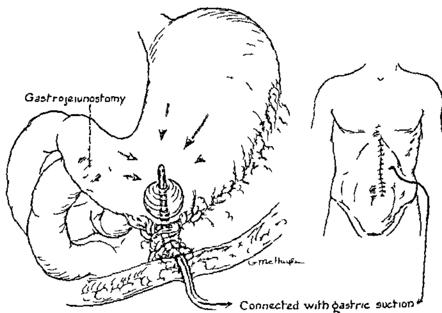


Fig 6 Diagram illustrating the method of decompressing the stomach post-operatively by means of a Foley bag introduced into fundus of the stomach Ten to fifteen cc of water is placed in the bag and the stomach infolded around the rubber catheter with several infolding catgut stitches Omentum is then wrapped around the catheter which is then led through the abdominal wall by a stab wound near the left costal margin

gastro intestinal decompression in post-operative treatment I believe that is a tragic mistake It is imperative to decompress the stomach after gastric vagotomy in the treatment of duodenal ulcer For some years we have been accomplishing this by placing a Foley bag in the fundus of the stomach through a gas trostomy opening at the time of operation (fig 6) The catheter connected with the bag is led through the abdominal wall through a small stab wound under the left costal margin. By this method prolonged decompression of the stomach can be achieved with little or no discomfort I have also made use of this method of gastric decompression in patients who have had extensive resec tions of the colon for malignant disease Other surgeons also have commented on the safety and convenience of this method It is not likely that knowledge gained through the work of Snow Murphy Gamble and others will ever be lost, but there is some hazard that it may not be adequately applied.

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ROENTGEN EXAMINATION OF THE COLON

FREDERIC E TEMPLETON MD *

PREFACE

THE following resume on Roentgen Examination of the Colon is primarily concerned with technique Illustrative lantern slides are taken from patients complaining of changes in bowel habits such as diarrhea and constipation Most clinicians refer patients having these complaints in order to determine the absence or presence of lesions In some patients neoplastic or inflammatory conditions are found but in most patients a diagnosis of normal colon is returned The lantern slides therefore illustrate physiologic variations in the normal as well as the abnormal colon

I INTRODUCTION

The roentgenologic examination of the colon changes More dependence is placed on films and less on fluoroscopy The change is dictated by a desire not only to increase diagnostic accuracy but to meet the current demands for a rapid examination which gives the most information for the least expenditure of time and money

The basic method should be standardized just as the roentgenologic examination of the chest the lumbar spine and the skull When standardization is accomplished patients will not be required to undergo so many repeated examinations with added radiation exposure as they move from doctor to doctor or clinic

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to clinic The progress of a lesion under medical management can be followed more accurately because the films have more comparative value

The method I present has been used in our office since 1946 It is modified from time to time but the basic approach is the same The method combines full filling of the colon high kilo voltage spot filming drainage by suction double contrast and post evacuation films into one continuous effort By using twin fluoroscopic filming units eight to twelve examinations an hour are done We schedule two examinations every fifteen minutes and often work in two or three extra patients during each hour Films are used freely because a lesion is rarely seen at fluoroscopy which does not show on the films Films also show lesions not seen at fluoroscopy and films require less radiation than pro longed fluoroscopy even when the image intensifier is used

In order to apply the method successfully it is necessary to understand the effects of muscular contraction and motility In general the colon lengthens as it distends with contrast medium and shortens often with disappearance of redundant loops with evacuation The tone and peristaltic activity vary with the pa tient and with the content temperature and rapidity of adminis tration of the enema The fold pattern differs with the degree of distention In general the mucosa is smooth when the colon distends Parallel or wavy folds appear when the colon contracts Parallel folds are caused by contraction of circular muscle and wavy folds by longitudinal muscle The patterns vary not only with the degree of contraction but with patients and in parts of the same colon

II PREPARATION AND MATERIALS

A clean colon is essential We place the patient on a bland diet during the forty eight hours prior to the examination The blander the diet the better Two ounces of castor oil are given the night before the examination and a tap water enema approx imately two hours or more before his appointment the following morning He eats no breakfast Breakfast stimulates peristalsis and forces material into the cecum from the small bowel after the castor oil runs its course Lately we have used Dulcolax®

with some success We are not yet ready to recommend it because our experience is limited

The apparatus is a three way valve reported by Addington and Templeton[1] The drainage side of the valve is connected to a standard Crane aspirator recessed into the wall next to the sink. The aspirator is commonly used for suction in hospitals and by ear nose and throat men

The barium mixture is a commercial preparation It makes little difference which as long as the mixture contains a good suspensory agent To each quart of barium mixture are added two ounces of one per cent A O T® (dioctyl sodium sulphasuccinate) and twenty milligrams of Lavema® (dihydroxydiphenylisatin) The A O T® is a wetting agent which prevents impaction and the Lavema® is a mucosal irritant that aids in evacuating the colon The consistency is determined by measuring the mixture so that the hydrometer reads between 30 and 35 Baume units Thick mixtures are necessary for good double contrast examinations A mixture measuring less than 30 Baume units seldom coats the bowel walls with barium

III THE EXAMINATION

The enema tube is inserted (if the patient states that he has difficulty holding the enema we use the Bardex self retaining catheter hooked to a special adapter) and the patient is placed in the supine position the right side elevated The rectum is observed as it distends with barium and as the barium passes the rectosigmoid the patient is rolled from side to side in order to see better this section of the colon A spot film is made of the region When the barium reaches the mid descending colon the enema is turned off The enema will continue to coast toward the splenic flexure The sigmoid contracts and the patient instead of straining to hold the enema relaxes If the sigmoid does not contract and the rectum remains distended drainage is instituted With drainage the colon shortens If the rectum overlaps

[1]Templeton F E and Addington E A Roentgenologic examination of the colon using drainage and negative pressure *J A M A* *145(10)* 702 704 March 1951

the sigmoid the collapse of the rectum uncovers the sigmoid Pressure is applied and spot films are made Pressure on the undistended sigmoid is one of the best methods I know to demonstrate polyps and diverticula I believe that close approximation of the walls which occurs when the colon collapses is more important than high kilovoltage in demonstrating polyps Certainly *this is true in the stomach and it should be true in the colon*

We work with from 90 to 100 kilovolts We have not gone to the higher voltages because of the protection problem

After the rectosigmoid is examined the enema is restarted and the head of the column *followed around to the hepatic flexure* Drainage is again instituted. The patient's left side is elevated in order to separate the overlapping loops of the splenic flexure The descending colon and splenic flexure are palpated and studied The drainage causes the patient's abdomen to relax Palpation is easier The patient is placed flat on his back and the transverse colon palpated During the examination of the splenic flexure the barium enema continues *to coast by gravity into the* ascending colon and cecum If this does not happen the enema is again started Barium is forced into the cecum Sometimes a few puffs of air instead of barium will do the job After the ascending colon fills the right side is raised This maneuver separates the arms of the hepatic flexure The cecum and ascending colon are palpated If barium has not entered the cecum barium may *be forced into it by palpation or by having the patient* sit up Often this is preferable to restarting the barium enema because of the discomfort caused by distention of the colon Sometimes these maneuvers are the only way of filling the cecum with barium if the cecum is already distended with air After the cecum fills the terminal ileum and appendix may fill Drainage is re instituted The patient relaxes and more time can be given to the examination of the cecum appendix and terminal ileum Spot views of these structures are routinely made Sometimes a mass evacuation contraction occurs and can be followed If the *contraction is not desired* a few *puffs of air often* cause enough back pressure to counteract the contraction If however the evacuation contraction makes the patient too uncomfortable

drainage is instituted Sometimes the severe mass contractions completely empty the colon When this happens more barium must be injected Air injected into a firmly contracted colon rarely results in good double contrast views The pattern is broken up by caking The best patterns are produced by distending the partially contracted colon with air After drainage and injection of air three films are made two with the patient supine—one with the right side raised and one with the left side raised The third film is made with the patient prone These views are not only of the double contrast variety but are of the fully distended colon as well We have learned to like these views better than those of the colon filled only with barium We think that they give more information After these three films the patient is sent to stool and returns for a post evacuation film This film completes the examination

If the colon is dirty and polyps are suspected lateral decubitus views are added along with an upright film These films are obtained before the patient goes to stool With proper equipment —that is a grid which can be attached to the side of a tilting table —only an extra minute or two are needed for the examination If the colon is extremely dirty the patient is sent to stool after the colon is filled with enema but before the large films are made In a high percentage of patients the colon empties completely The examination can be redone with the assurance of a clean bowel

We have become so accustomed to using air as a part of our examination that we often examine patients after proctoscopic examination Patients usually appreciate this because not only does it save them an extra trip but if they are in the hospital it saves them the cost of an added day's stay The amount of gas in the colon does not bother us We spread the barium by turning the patient from the prone to the supine and back again by sitting him up or by tilting the table

General Questions and Answers

Moderator

J Alfred Rider, M D Ph D
Assistant Professor of Medicine
University of California School of Medicine
San Francisco California

Panel Members

Lester R Dragstedt M D Ph D Professor of Surgery University of Chicago School of Medicine

Gordon McHardy M D Associate Professor of Medicine Louisiana State University Medical School

Roger G Simpson M D Associate Clinical Professor of Medicine University of California Medical Center San Francisco

Frederick Steigmann M D Chief of Gastroenterology Service Cook County Hospital Chicago

Frederick E Templeton M D Clinical Professor of Radiology University of Washington School of Medicine Seattle

Question What should be the medical management of a young patient a middle aged patient and an elderly patient with one vague gastrointestinal complaint such as excessive belching without relation to meals and in whose gastric content no free hydrochloric acid is found? In addition the results of serial x ray examination of the upper and lower gastrointestinal tract and gall bladder are negative and the results of hematological studies indicate that the blood is normal

Is carcinoma of the stomach likely to develop in this type of patient Would you examine him roentgenographically or gas

troscopically every six to twelve months? Would you treat him with hydrochloric acid or vitamin B_{12}?

Doctor McHardy I think we look on all patients with an established achlorhydria as possible pre-cancer individuals and they should be watched more closely than the average To some degree these patient are more likely to have carcinoma of the stomach than the average

I think I would advise this type of patient to have an upper gastrointestinal tract x ray annually and I would couple that with cytology rather than gastroscopy I would only add gastroscopy if there were some further question and gastroscopy might complement the radiological studies I say cytology rather than gastroscopy from the viewpoint of trauma to the patient and because gastroscopy is not that conclusive a procedure I also assume that the patient was gastroscoped at least one time during the diagnostic summarization

I would be inclined to treat the patient with hydrochloric acid if it benefits him in relation to the vague gastrointestinal complaint that you described With the use of vitamin B_{12} we have not noticed any remarkable cytological or secretory change but we are inclined to use it with patients who have gastric atrophy or achlorhydria

Question This morning we presented a case of functional constipation and Doctor Steigman spoke very informatively about some new laxative preparations Bearing in mind the psychiatric findings relating to the patient with functional constipation do you think that it would be better to treat her practically with a laxative such as Senokot® or do you think it would be better for her to receive prolonged psychiatric care?

Doctor Steigman I think that a patient like this should be treated according to the way I tried to describe this morning She should definitely first be investigated psychiatrically because she is a psychiatric problem Of course if she refuses psychiatric examination you cannot do anything but she needs it and that is part of her problem *She fits very well into the type of problem* category that Doctor Hurst described so well as nervous depres

sion causing sluggishness of the colon or colic constipation She also should be induced to follow a good diet, and use laxatives as a complementary measure until she can perhaps get her bowel more regulated Of course the laxative alone is not going to do anything for her She must have a combination of all the factors Now in her case the fact that she has colic constipation means that the progress of fecal material through the colon is slow and she would benefit by a laxative like Senokot® which is something of a stimulant to the myenteric plexus and to the musculature of the colon

Question Does Senokot® stimulate the small bowel as well as the large bowel?

Doctor Steigman From the experiments done in Europe and from some of our own work we have not noticed any action on the small bowel Apparently it stimulates only the large bowel

Question Is urecholine effective in treating ptosis of the stomach in neurotic individuals?

Doctor Simpson Well I think the answer is no You might get one complete return of tone to a stomach by using urecholine but this is not a practical method of day to-day treatment I don t think you would do the patient any good You would probably increase tone too much and the patient would have a lot of discomfort and cramping Ptosis after all is a relative anatomical condition and I don t think you would change it at all with this method of treatment

Question Do you think it is important to treat a person with ptosis of the stomach?

Doctor Simpson I think ptosis is a normal finding and when it is reported or discovered by a patient or he hears about it I think you should make every effort to sit down and talk to him about it and explain that it is a normal variation a common thing and of no importance at all

Question Is there any surgical treatment for ptosis?

Doctor Dragstedt That was abandoned a long time ago

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Doctor Simpson I think *ptosis is a normal finding* and when it is reported or discovered by a patient or he hears about it I think you should make every effort to sit down and talk to him about it and explain that it is a normal variation a common thing and of no importance at all

Question Is there any surgical treatment for ptosis?

Doctor Dragstedt That was abandoned a long time ago

Operations used to be performed on patients with ptosis but not any longer

Question Doctor Templeton do you consider that there are any specific roentgenologic findings typical of the so called irritable bowel? Do you see fluoroscopic evidence of sigmoid spasm or hypermotility in this syndrome?

Doctor Templeton No I dont consider that there are any specific roentgenological findings typical of the so-called irritable bowel I know that there are statements in medical literature that the small colon which fills rapidly is typical of the colon of the irritable bowel particularly if this causes distress If the barium enema in the colon reproduces the patients distress then you might say yes but it isnt the x ray appearance that is doing that It is a symptomatic thing We see many of these colons in patients with an irritable bowel but we also see them in other people who do not have an irritable bowel—for instance when we are examining because of blood in the stool and not because of an irritable bowel

Question Do you see evidence of sigmoid spasm or hyper motility in this syndrome?

Doctor Templeton No I have not but that may be because of the way we prepare patients colons and the way we do the roentgenologic examination

Question Is it worthwhile to insist that a patient have a chest x ray every year if he has had a sub total gastrectomy and if there is no demonstrable free hydrochloric acid in his gastric content? It is assumed that patients with total or sub total gastrectomies may be more likely than normal persons to develop infections caused by acid fast bacilli

Doctor Dragstedt Yes I think that the studies that have been made indicate that one of the disadvantages of sub total gastric resection for the treatment of benign ulcer disease is the increased incidence of tuberculosis in these patients It is not a frequent complication but it does appear in any large statistical study of the results of gastric resections This nutritive impair

ment in duodenal ulcer patients who have had a sub total gastric resection is one of the findings that interested me in trying to develop a more conservative surgical procedure for the treatement of duodenal ulcer